Dossier zur Nutzenbewertung gemäß § 35a SGB V

Deutivacaftor/Tezacaftor/Vanzacaftor (Alyftrek®)

Vertex Pharmaceuticals (Ireland) Limited

Anhang 4-G

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

Zusatzanalysen für das Nutzendossier

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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Table 1.2.1.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52
Full Analysis Set

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

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

Table 1.2.1.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52
Full Analysis Set

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

-CI: Confidence interval.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
-Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
-*Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years).
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Table 1.2.1.7.1
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

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

-CI: Confidence interval.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
-Subjects without any protocol-defined pulmonary exacerbation requiring hospitalization during the PEx analysis period were censored at the PEx analysis period end date.
-*Cox regression: time is the time-to-first pulmonary exacerbation requiring hospitalization or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years).
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Table 1.2.1.8.1
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

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

-CI: Confidence interval.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
-Subjects without any protocol-defined pulmonary exacerbation requiring IV Antibiotics during the PEx analysis period were censored at the PEx analysis period end date.
-*Cox regression: time is the time-to-first pulmonary exacerbation requiring IV Antibiotics or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years).
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Table 1.2.1.9.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline	189 (93.56)	187 (95.41)
Week 8	191 (94.55)	188 (95.92)
Absolute Change at Week 8	188 (93.07)	185 (94.39)
Week 16	189 (93.56)	189 (96.43)
Absolute Change at Week 16	186 (92.08)	186 (94.90)
Week 24	189 (93.56)	188 (95.92)
Absolute Change at Week 24	186 (92.08)	185 (94.39)
Week 52	184 (91.09)	179 (91.33)
Absolute Change at Week 52	181 (89.60)	176 (89.80)
Through Week 52	189 (93.56)	189 (96.43)
Absolute Change through Week 52	186 (92.08)	186 (94.90)

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

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

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

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

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

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

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

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline	189 (93.56)	186 (94.90)
Week 8	190 (94.06)	188 (95.92)
Absolute Change at Week 8	187 (92.57)	184 (93.88)
Week 16	189 (93.56)	189 (96.43)
Absolute Change at Week 16	186 (92.08)	185 (94.39)
Week 24	189 (93.56)	187 (95.41)
Absolute Change at Week 24	186 (92.08)	183 (93.37)
Week 52	183 (90.59)	179 (91.33)
Absolute Change at Week 52	180 (89.11)	175 (89.29)
Through Week 52	189 (93.56)	189 (96.43)
Absolute Change through Week 52	186 (92.08)	185 (94.39)

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

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

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

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

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

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

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

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

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

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

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

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline	189 (93.56)	187 (95.41)
Week 8	191 (94.55)	188 (95.92)
Absolute Change at Week 8	188 (93.07)	185 (94.39)
Week 16	189 (93.56)	189 (96.43)
Absolute Change at Week 16	186 (92.08)	186 (94.90)
Week 24	189 (93.56)	188 (95.92)
Absolute Change at Week 24	186 (92.08)	185 (94.39)
Week 52	184 (91.09)	179 (91.33)
Absolute Change at Week 52	181 (89.60)	176 (89.80)
Through Week 52	189 (93.56)	189 (96.43)
Absolute Change through Week 52	186 (92.08)	186 (94.90)

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

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

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

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline	189 (93.56)	187 (95.41)
Week 8	190 (94.06)	188 (95.92)
Absolute Change at Week 8	187 (92.57)	185 (94.39)
Week 16	189 (93.56)	189 (96.43)
Absolute Change at Week 16	186 (92.08)	186 (94.90)
Week 24	189 (93.56)	187 (95.41)
Absolute Change at Week 24	186 (92.08)	184 (93.88)
Week 52	183 (90.59)	179 (91.33)
Absolute Change at Week 52	180 (89.11)	176 (89.80)
Through Week 52	189 (93.56)	189 (96.43)
Absolute Change through Week 52	186 (92.08)	186 (94.90)

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

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

Version: Parents/Caregivers Version

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

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

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

Version: Parents/Caregivers Version

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

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

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

Version: Parents/Caregivers Version

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

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

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

Version: Parents/Caregivers Version

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

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

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

Version: Parents/Caregivers
Domain: Respiration

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

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

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

Version: Parents/Caregivers
Domain: Body

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

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

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

Version: Parents/Caregivers
Domain: Digestion

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

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

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

Version: Parents/Caregivers
Domain: Eat

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

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

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

Version: Parents/Caregivers
Domain: Emotion

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

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

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

Version: Parents/Caregivers
Domain: Health Perceptions

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

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

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

Version: Parents/Caregivers
Domain: Physical

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

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

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

Version: Parents/Caregivers
Domain: School

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

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

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

Version: Parents/Caregivers
Domain: Treatment Burden

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

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

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

Version: Parents/Caregivers
Domain: Vitality

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

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

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

Version: Parents/Caregivers
Domain: Weight

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	189	187
Mean (SD)	71.13 (19.24)	73.92 (19.53)
Week 8 (MMRM)		
n	189	183
LS mean (SE)	70.41 (1.38)	72.98 (1.40)
95% CI of LS mean	(67.69, 73.13)	(70.21, 75.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.56 (-1.31, 6.44)
Absolute Change at Week 8 (MMRM)		
n	186	181
LS mean (SE)	-1.03 (1.03)	-0.71 (1.04)
95% CI of LS mean	(-3.06, 1.00)	(-2.76, 1.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.32 (-2.57, 3.20)
Week 16 (MMRM)		
n	187	184
LS mean (SE)	71.40 (1.46)	72.82 (1.47)
95% CI of LS mean	(68.54, 74.26)	(69.93, 75.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.42 (-2.65, 5.49)

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

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

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

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 16 (MMRM)		
n	184	182
LS mean (SE)	-0.31 (1.06)	-0.81 (1.06)
95% CI of LS mean	(-2.38, 1.77)	(-2.90, 1.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.50 (-3.45, 2.45)
Week 24 (MMRM)		
n	187	183
LS mean (SE)	70.33 (1.49)	74.04 (1.51)
95% CI of LS mean	(67.39, 73.27)	(71.07, 77.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.72 (-0.46, 7.89)
Absolute Change at Week 24 (MMRM)		
n	184	181
LS mean (SE)	-1.28 (1.04)	0.20 (1.05)
95% CI of LS mean	(-3.32, 0.76)	(-1.86, 2.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.48 (-1.42, 4.38)
Week 52		
n	184	179
Mean (SD)	72.68 (19.98)	74.98 (20.05)

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

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

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

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52		
n	181	176
Mean (SD)	1.20 (12.89)	1.07 (15.01)
Week 52 (MMRM)		
n	182	175
LS mean (SE)	73.06 (1.44)	75.21 (1.46)
95% CI of LS mean	(70.23, 75.88)	(72.34, 78.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.15 (-1.88, 6.18)
Absolute Change at Week 52 (MMRM)		
n	179	173
LS mean (SE)	1.43 (1.04)	1.28 (1.06)
95% CI of LS mean	(-0.62, 3.48)	(-0.80, 3.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-3.06, 2.78)

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

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

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

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change through Week 52 (MMRM)		
n	184	182
LS mean (SE)	-0.05 (0.83)	0.22 (0.84)
95% CI of LS mean	(-1.69, 1.58)	(-1.42, 1.87)
P-value within Treatment	0.9481	0.7894
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.28 (-2.04, 2.60)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8139
Hedges' G (SE)		0.02 (0.10)
Hedges' 95% CI		(-0.18, 0.23)
Hedges' P-value		0.8138

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	189	186
Mean (SD)	87.65 (16.92)	87.37 (15.77)
Week 8 (MMRM)		
n	188	183
LS mean (SE)	87.07 (1.09)	87.74 (1.10)
95% CI of LS mean	(84.93, 89.21)	(85.57, 89.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.67 (-2.38, 3.72)
Absolute Change at Week 8 (MMRM)		
n	185	180
LS mean (SE)	-0.62 (0.94)	0.51 (0.96)
95% CI of LS mean	(-2.48, 1.23)	(-1.37, 2.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.14 (-1.51, 3.78)
Week 16 (MMRM)		
n	187	184
LS mean (SE)	85.91 (1.15)	88.82 (1.17)
95% CI of LS mean	(83.64, 88.18)	(86.52, 91.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.90 (-0.32, 6.13)

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

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

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

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 16 (MMRM)		
n	184	181
LS mean (SE)	-1.62 (1.06)	2.01 (1.07)
95% CI of LS mean	(-3.72, 0.47)	(-0.11, 4.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.63 (0.66, 6.60)
Week 24 (MMRM)		
n	187	182
LS mean (SE)	86.89 (1.11)	88.19 (1.12)
95% CI of LS mean	(84.71, 89.07)	(85.98, 90.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.30 (-1.81, 4.41)
Absolute Change at Week 24 (MMRM)		
n	184	179
LS mean (SE)	-0.85 (1.01)	1.16 (1.03)
95% CI of LS mean	(-2.84, 1.14)	(-0.86, 3.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.01 (-0.83, 4.84)
Week 52		
n	183	179
Mean (SD)	88.80 (14.76)	88.73 (14.77)

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

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

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

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52		
n	180	175
Mean (SD)	1.06 (12.30)	1.81 (14.65)
Week 52 (MMRM)		
n	181	175
LS mean (SE)	88.69 (1.08)	88.71 (1.10)
95% CI of LS mean	(86.57, 90.82)	(86.56, 90.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.02 (-3.01, 3.05)
Absolute Change at Week 52 (MMRM)		
n	178	172
LS mean (SE)	1.05 (1.01)	1.59 (1.02)
95% CI of LS mean	(-0.94, 3.03)	(-0.43, 3.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.54 (-2.29, 3.37)

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

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

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

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change through Week 52 (MMRM)		
n	184	181
LS mean (SE)	-0.47 (0.87)	1.58 (0.88)
95% CI of LS mean	(-2.18, 1.23)	(-0.14, 3.31)
P-value within Treatment	0.5841	0.0717
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.06 (-0.37, 4.48)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0959
Hedges' G (SE)		0.17 (0.10)
Hedges' 95% CI		(-0.03, 0.38)
Hedges' P-value		0.0964

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	189	187
Mean (SD)	66.78 (17.71)	69.65 (20.07)
Week 8 (MMRM)		
n	189	183
LS mean (SE)	65.05 (1.41)	67.84 (1.43)
95% CI of LS mean	(62.28, 67.81)	(65.03, 70.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.79 (-1.15, 6.74)
Absolute Change at Week 8 (MMRM)		
n	186	181
LS mean (SE)	-2.04 (1.28)	-1.62 (1.30)
95% CI of LS mean	(-4.56, 0.48)	(-4.17, 0.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-3.17, 4.02)
Week 16 (MMRM)		
n	187	184
LS mean (SE)	64.62 (1.49)	67.76 (1.50)
95% CI of LS mean	(61.70, 67.54)	(64.81, 70.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.14 (-1.01, 7.30)

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

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

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

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 16 (MMRM)		
n	184	182
LS mean (SE)	-2.25 (1.20)	-1.44 (1.21)
95% CI of LS mean	(-4.61, 0.11)	(-3.82, 0.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.81 (-2.54, 4.16)
Week 24 (MMRM)		
n	187	183
LS mean (SE)	64.31 (1.51)	67.55 (1.53)
95% CI of LS mean	(61.34, 67.28)	(64.55, 70.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.24 (-0.98, 7.47)
Absolute Change at Week 24 (MMRM)		
n	184	181
LS mean (SE)	-2.70 (1.23)	-2.00 (1.24)
95% CI of LS mean	(-5.13, -0.28)	(-4.45, 0.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.70 (-2.75, 4.15)
Week 52		
n	184	179
Mean (SD)	66.89 (18.61)	68.95 (20.02)

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

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

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

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52		
n	181	176
Mean (SD)	-0.26 (14.86)	-0.62 (18.13)
Week 52 (MMRM)		
n	182	175
LS mean (SE)	66.76 (1.41)	69.02 (1.44)
95% CI of LS mean	(63.98, 69.54)	(66.20, 71.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.26 (-1.71, 6.22)
Absolute Change at Week 52 (MMRM)		
n	179	173
LS mean (SE)	-0.33 (1.24)	-0.59 (1.26)
95% CI of LS mean	(-2.77, 2.10)	(-3.06, 1.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-3.72, 3.22)

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

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

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

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change through Week 52 (MMRM)		
n	184	182
LS mean (SE)	-1.76 (1.00)	-1.34 (1.01)
95% CI of LS mean	(-3.73, 0.20)	(-3.33, 0.64)
P-value within Treatment	0.0786	0.1833
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.42 (-2.37, 3.21)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7681
Hedges' G (SE)		0.03 (0.10)
Hedges' 95% CI		(-0.17, 0.24)
Hedges' P-value		0.7680

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

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

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

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	189	187
Mean (SD)	84.83 (26.95)	82.35 (28.98)
Week 8 (MMRM)		
n	188	183
LS mean (SE)	85.44 (1.94)	83.20 (1.97)
95% CI of LS mean	(81.62, 89.26)	(79.33, 87.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.24 (-7.68, 3.20)
Absolute Change at Week 8 (MMRM)		
n	185	181
LS mean (SE)	0.51 (1.55)	1.13 (1.57)
95% CI of LS mean	(-2.54, 3.56)	(-1.95, 4.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.62 (-3.72, 4.97)
Week 16 (MMRM)		
n	187	184
LS mean (SE)	82.31 (2.10)	82.85 (2.13)
95% CI of LS mean	(78.17, 86.44)	(78.67, 87.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.54 (-5.34, 6.42)

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

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

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

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 16 (MMRM)		
n	184	182
LS mean (SE)	-2.69 (1.78)	0.76 (1.79)
95% CI of LS mean	(-6.18, 0.81)	(-2.76, 4.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.45 (-1.52, 8.41)
Week 24 (MMRM)		
n	187	182
LS mean (SE)	84.81 (2.09)	82.72 (2.12)
95% CI of LS mean	(80.69, 88.92)	(78.55, 86.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.09 (-7.94, 3.77)
Absolute Change at Week 24 (MMRM)		
n	184	180
LS mean (SE)	0.03 (1.80)	0.62 (1.82)
95% CI of LS mean	(-3.52, 3.58)	(-2.96, 4.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.59 (-4.45, 5.64)
Week 52		
n	183	179
Mean (SD)	86.16 (24.76)	82.50 (27.21)

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

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

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

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52		
n	180	176
Mean (SD)	1.11 (24.89)	-0.19 (21.82)
Week 52 (MMRM)		
n	181	175
LS mean (SE)	85.54 (1.95)	81.59 (1.98)
95% CI of LS mean	(81.70, 89.37)	(77.70, 85.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.94 (-9.41, 1.52)
Absolute Change at Week 52 (MMRM)		
n	178	173
LS mean (SE)	0.62 (1.75)	-0.56 (1.77)
95% CI of LS mean	(-2.82, 4.06)	(-4.04, 2.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.17 (-6.07, 3.72)

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

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

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

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change through Week 52 (MMRM)		
n	184	182
LS mean (SE)	-0.68 (1.51)	0.28 (1.53)
95% CI of LS mean	(-3.65, 2.30)	(-2.73, 3.28)
P-value within Treatment	0.6535	0.8566
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.96 (-3.27, 5.18)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6569
Hedges' G (SE)		0.05 (0.10)
Hedges' 95% CI		(-0.16, 0.25)
Hedges' P-value		0.6569

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

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

Version: Parents/Caregivers Version
Domain: Body

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

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

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

Version: Parents/Caregivers Version
Domain: Body

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

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

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

Version: Parents/Caregivers Version
Domain: Body

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

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

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

Version: Parents/Caregivers Version
Domain: Body

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

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

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

Version: Parents/Caregivers Version
Domain: Digestion

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

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

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

Version: Parents/Caregivers Version
Domain: Digestion

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

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

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

Version: Parents/Caregivers Version
Domain: Digestion

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

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

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

Version: Parents/Caregivers Version
Domain: Digestion

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

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

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

Version: Parents/Caregivers Version
Domain: Eat

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

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

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

Version: Parents/Caregivers Version
Domain: Eat

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

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

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

Version: Parents/Caregivers Version
Domain: Eat

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

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

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

Version: Parents/Caregivers Version
Domain: Eat

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

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

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

Version: Parents/Caregivers Version
Domain: Emotion

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

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

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

Version: Parents/Caregivers Version
Domain: Emotion

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

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

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

Version: Parents/Caregivers Version
Domain: Emotion

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

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

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

Version: Parents/Caregivers Version
Domain: Emotion

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

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

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

Version: Parents/Caregivers Version
Domain: Health Perceptions

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

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

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

Version: Parents/Caregivers Version
Domain: Health Perceptions

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

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

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

Version: Parents/Caregivers Version
Domain: Health Perceptions

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

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

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

Version: Parents/Caregivers Version
Domain: Health Perceptions

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

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

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

Version: Parents/Caregivers Version
Domain: Physical

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

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

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

Version: Parents/Caregivers Version
Domain: Physical

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

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

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

Version: Parents/Caregivers Version
Domain: Physical

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

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

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

Version: Parents/Caregivers Version
Domain: Physical

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

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

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

Version: Parents/Caregivers Version
Domain: School

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

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

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

Version: Parents/Caregivers Version
Domain: School

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

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

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

Version: Parents/Caregivers Version
Domain: School

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

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

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

Version: Parents/Caregivers Version
Domain: School

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

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

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

Version: Parents/Caregivers Version
Domain: Treatment Burden

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

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

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

Version: Parents/Caregivers Version
Domain: Treatment Burden

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

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

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

Version: Parents/Caregivers Version
Domain: Treatment Burden

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

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

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

Version: Parents/Caregivers Version
Domain: Treatment Burden

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

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

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

Version: Parents/Caregivers Version
Domain: Vitality

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

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

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

Version: Parents/Caregivers Version
Domain: Vitality

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

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

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

Version: Parents/Caregivers Version
Domain: Vitality

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

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

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

Version: Parents/Caregivers Version
Domain: Vitality

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

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

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

Version: Parents/Caregivers Version
Domain: Weight

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

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

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

Version: Parents/Caregivers Version
Domain: Weight

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

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

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

Version: Parents/Caregivers Version
Domain: Weight

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

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

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

Version: Parents/Caregivers Version
Domain: Weight

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

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

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

Domain: Effectiveness

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

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

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

Domain: Effectiveness

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

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

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

Domain: Side Effects

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

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

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

Domain: Side Effects

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

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

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

Domain: Convenience

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

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

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

Domain: Convenience

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

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

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

Domain: Global Satisfaction

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

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

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

Domain: Global Satisfaction

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

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

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

Domain: Effectiveness

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

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

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

Domain: Side Effects

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

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

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

Domain: Convenience

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

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

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

Domain: Global Satisfaction

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

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

Table 1.2.1.13.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	196	191
Mean (SD)	10.39 (3.83)	10.23 (3.78)
Week 4 (MMRM)		
n	191	190
LS mean (SE)	10.05 (0.26)	10.12 (0.26)
95% CI of LS mean	(9.54, 10.56)	(9.60, 10.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-0.66, 0.79)
Absolute Change at Week 4 (MMRM)		
n	185	185
LS mean (SE)	-0.26 (0.17)	-0.15 (0.17)
95% CI of LS mean	(-0.58, 0.07)	(-0.47, 0.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.11 (-0.35, 0.57)
Week 24 (MMRM)		
n	193	178
LS mean (SE)	10.39 (0.28)	10.35 (0.29)
95% CI of LS mean	(9.83, 10.95)	(9.78, 10.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-0.84, 0.76)

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

Table 1.2.1.13.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 24 (MMRM)		
n	188	174
LS mean (SE)	0.08 (0.21)	0.12 (0.22)
95% CI of LS mean	(-0.33, 0.49)	(-0.31, 0.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.04 (-0.55, 0.63)
Week 52		
n	188	181
Mean (SD)	10.05 (3.79)	10.11 (3.69)
Absolute Change at Week 52		
n	182	176
Mean (SD)	-0.41 (2.80)	-0.22 (3.12)
Week 52 (MMRM)		
n	186	178
LS mean (SE)	9.98 (0.27)	10.18 (0.27)
95% CI of LS mean	(9.46, 10.51)	(9.65, 10.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.20 (-0.55, 0.95)

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

Table 1.2.1.13.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52 (MMRM)		
n	180	173
LS mean (SE)	-0.37 (0.22)	-0.11 (0.23)
95% CI of LS mean	(-0.81, 0.06)	(-0.55, 0.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.26 (-0.36, 0.88)
Absolute Change through Week 52 (MMRM)		
n	189	180
LS mean (SE)	-0.15 (0.19)	0.01 (0.19)
95% CI of LS mean	(-0.51, 0.22)	(-0.37, 0.38)
P-value within Treatment	0.4351	0.9769
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-0.38, 0.68)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5715
Hedges' G (SE)		0.06 (0.10)
Hedges' 95% CI		(-0.15, 0.26)
Hedges' P-value		0.5714

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

Table 1.2.1.13.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Physical Activity

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	196	190
Mean (SD)	11.45 (4.20)	11.42 (4.43)
Week 4 (MMRM)		
n	190	189
LS mean (SE)	11.49 (0.29)	11.20 (0.30)
95% CI of LS mean	(10.91, 12.07)	(10.62, 11.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.29 (-1.11, 0.53)
Absolute Change at Week 4 (MMRM)		
n	184	183
LS mean (SE)	0.14 (0.23)	-0.25 (0.23)
95% CI of LS mean	(-0.31, 0.59)	(-0.70, 0.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.39 (-1.03, 0.25)
Week 24 (MMRM)		
n	193	178
LS mean (SE)	11.79 (0.32)	11.42 (0.34)
95% CI of LS mean	(11.15, 12.43)	(10.76, 12.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.37 (-1.29, 0.55)

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

Table 1.2.1.13.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Physical Activity

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 24 (MMRM)		
n	188	174
LS mean (SE)	0.44 (0.25)	0.00 (0.26)
95% CI of LS mean	(-0.05, 0.93)	(-0.51, 0.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.44 (-1.14, 0.26)
Week 52		
n	188	181
Mean (SD)	11.59 (4.20)	11.23 (4.08)
Absolute Change at Week 52		
n	182	175
Mean (SD)	0.13 (3.26)	-0.29 (3.80)
Week 52 (MMRM)		
n	186	178
LS mean (SE)	11.51 (0.29)	11.30 (0.30)
95% CI of LS mean	(10.94, 12.09)	(10.71, 11.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-1.04, 0.61)

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

Table 1.2.1.13.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Physical Activity

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52 (MMRM)		
n	180	172
LS mean (SE)	0.13 (0.26)	-0.18 (0.27)
95% CI of LS mean	(-0.39, 0.65)	(-0.71, 0.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-1.05, 0.43)
Absolute Change through Week 52 (MMRM)		
n	189	179
LS mean (SE)	0.28 (0.21)	-0.09 (0.22)
95% CI of LS mean	(-0.13, 0.70)	(-0.52, 0.33)
P-value within Treatment	0.1772	0.6651
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-0.97, 0.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2110
Hedges' G (SE)		-0.13 (0.10)
Hedges' 95% CI		(-0.34, 0.07)
Hedges' P-value		0.2114

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

Table 1.2.1.13.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Social Activity

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	196	191
Mean (SD)	5.38 (2.43)	5.24 (2.21)
Week 4 (MMRM)		
n	191	189
LS mean (SE)	5.18 (0.15)	5.15 (0.15)
95% CI of LS mean	(4.89, 5.47)	(4.86, 5.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-0.45, 0.39)
Absolute Change at Week 4 (MMRM)		
n	185	184
LS mean (SE)	-0.19 (0.12)	-0.10 (0.12)
95% CI of LS mean	(-0.42, 0.04)	(-0.32, 0.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.09 (-0.23, 0.41)
Week 24 (MMRM)		
n	193	178
LS mean (SE)	5.31 (0.17)	5.29 (0.17)
95% CI of LS mean	(4.98, 5.64)	(4.96, 5.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.02 (-0.48, 0.45)

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

Table 1.2.1.13.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Social Activity

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 24 (MMRM)		
n	188	174
LS mean (SE)	-0.05 (0.14)	0.05 (0.15)
95% CI of LS mean	(-0.33, 0.23)	(-0.24, 0.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-0.30, 0.50)
Week 52		
n	188	181
Mean (SD)	5.16 (2.32)	5.14 (2.27)
Absolute Change at Week 52		
n	182	176
Mean (SD)	-0.25 (1.52)	-0.13 (2.10)
Week 52 (MMRM)		
n	186	178
LS mean (SE)	5.15 (0.16)	5.14 (0.16)
95% CI of LS mean	(4.83, 5.47)	(4.81, 5.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.02 (-0.47, 0.44)

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

Table 1.2.1.13.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Social Activity

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52 (MMRM)		
n	180	173
LS mean (SE)	-0.22 (0.13)	-0.12 (0.14)
95% CI of LS mean	(-0.48, 0.04)	(-0.39, 0.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-0.28, 0.48)
Absolute Change through Week 52 (MMRM)		
n	189	180
LS mean (SE)	-0.13 (0.12)	-0.03 (0.13)
95% CI of LS mean	(-0.38, 0.11)	(-0.28, 0.21)
P-value within Treatment	0.2764	0.7858
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-0.25, 0.45)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5712
Hedges' G (SE)		0.06 (0.10)
Hedges' 95% CI		(-0.15, 0.26)
Hedges' P-value		0.5712

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

Table 1.2.1.13.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Emotional

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	196	191
Mean (SD)	7.23 (3.14)	6.95 (2.93)
Week 4 (MMRM)		
n	192	190
LS mean (SE)	7.01 (0.20)	6.92 (0.20)
95% CI of LS mean	(6.62, 7.40)	(6.53, 7.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.65, 0.46)
Absolute Change at Week 4 (MMRM)		
n	186	185
LS mean (SE)	-0.16 (0.15)	-0.11 (0.15)
95% CI of LS mean	(-0.45, 0.12)	(-0.40, 0.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.06 (-0.35, 0.46)
Week 24 (MMRM)		
n	193	179
LS mean (SE)	7.17 (0.22)	6.93 (0.22)
95% CI of LS mean	(6.74, 7.60)	(6.49, 7.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-0.85, 0.37)

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

Table 1.2.1.13.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Emotional

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 24 (MMRM)		
n	188	175
LS mean (SE)	0.00 (0.20)	0.00 (0.21)
95% CI of LS mean	(-0.39, 0.39)	(-0.40, 0.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-0.56, 0.56)
Week 52		
n	188	181
Mean (SD)	6.93 (2.95)	6.76 (2.68)
Absolute Change at Week 52		
n	182	176
Mean (SD)	-0.34 (2.23)	-0.24 (2.76)
Week 52 (MMRM)		
n	186	178
LS mean (SE)	6.89 (0.20)	6.79 (0.21)
95% CI of LS mean	(6.49, 7.29)	(6.39, 7.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-0.67, 0.47)

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

Table 1.2.1.13.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Emotional

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52 (MMRM)		
n	180	173
LS mean (SE)	-0.32 (0.19)	-0.19 (0.19)
95% CI of LS mean	(-0.69, 0.04)	(-0.56, 0.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-0.39, 0.66)
Absolute Change through Week 52 (MMRM)		
n	189	180
LS mean (SE)	-0.16 (0.17)	-0.09 (0.17)
95% CI of LS mean	(-0.49, 0.17)	(-0.44, 0.25)
P-value within Treatment	0.3461	0.5907
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-0.41, 0.54)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7842
Hedges' G (SE)		0.03 (0.10)
Hedges' 95% CI		(-0.18, 0.23)
Hedges' P-value		0.7841

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

Table 1.2.1.13.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Work/School Limitation

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	196	190
Mean (SD)	5.06 (2.24)	4.97 (2.10)
Week 4 (MMRM)		
n	191	189
LS mean (SE)	4.92 (0.14)	4.82 (0.14)
95% CI of LS mean	(4.64, 5.20)	(4.53, 5.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-0.51, 0.29)
Absolute Change at Week 4 (MMRM)		
n	185	183
LS mean (SE)	-0.09 (0.10)	-0.18 (0.11)
95% CI of LS mean	(-0.29, 0.12)	(-0.38, 0.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.38, 0.20)
Week 24 (MMRM)		
n	193	178
LS mean (SE)	5.05 (0.16)	4.93 (0.16)
95% CI of LS mean	(4.74, 5.36)	(4.61, 5.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.12 (-0.56, 0.32)

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

Table 1.2.1.13.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Work/School Limitation

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 24 (MMRM)		
n	188	174
LS mean (SE)	0.03 (0.12)	-0.05 (0.12)
95% CI of LS mean	(-0.20, 0.25)	(-0.28, 0.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-0.40, 0.26)
Week 52		
n	188	181
Mean (SD)	4.96 (2.04)	4.82 (2.03)
Absolute Change at Week 52		
n	182	175
Mean (SD)	-0.12 (1.66)	-0.24 (1.93)
Week 52 (MMRM)		
n	186	178
LS mean (SE)	4.94 (0.14)	4.82 (0.15)
95% CI of LS mean	(4.65, 5.22)	(4.53, 5.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.12 (-0.53, 0.29)

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

Table 1.2.1.13.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Work/School Limitation

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52 (MMRM)		
n	180	172
LS mean (SE)	-0.11 (0.13)	-0.20 (0.14)
95% CI of LS mean	(-0.37, 0.16)	(-0.47, 0.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.47, 0.28)
Absolute Change through Week 52 (MMRM)		
n	189	179
LS mean (SE)	-0.04 (0.11)	-0.12 (0.11)
95% CI of LS mean	(-0.26, 0.18)	(-0.34, 0.10)
P-value within Treatment	0.7155	0.2779
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-0.39, 0.23)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6009
Hedges' G (SE)		-0.05 (0.10)
Hedges' 95% CI		(-0.26, 0.15)
Hedges' P-value		0.6009

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

Table 1.2.1.13.1.1
Study VX21-121-102: Compliance Rate for CF-IQ by Visit (All Domains)
Full Analysis Set

Domain: Control and Burden of CF Treatment

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline	196 (97.03)	191 (97.45)
Week 4	193 (95.54)	195 (99.49)
Absolute Change at Week 4	187 (92.57)	190 (96.94)
Week 24	195 (96.53)	183 (93.37)
Absolute Change at Week 24	190 (94.06)	179 (91.33)
Week 52	188 (93.07)	181 (92.35)
Absolute Change at Week 52	182 (90.10)	176 (89.80)
Through Week 52	197 (97.52)	190 (96.94)
Absolute Change through Week 52	191 (94.55)	185 (94.39)

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

Table 1.2.1.13.1.1
Study VX21-121-102: Compliance Rate for CF-IQ by Visit (All Domains)
Full Analysis Set

Domain: Physical Activity

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline	196 (97.03)	190 (96.94)
Week 4	192 (95.05)	194 (98.98)
Absolute Change at Week 4	186 (92.08)	188 (95.92)
Week 24	195 (96.53)	183 (93.37)
Absolute Change at Week 24	190 (94.06)	179 (91.33)
Week 52	188 (93.07)	181 (92.35)
Absolute Change at Week 52	182 (90.10)	175 (89.29)
Through Week 52	197 (97.52)	190 (96.94)
Absolute Change through Week 52	191 (94.55)	184 (93.88)

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

Table 1.2.1.13.1.1
Study VX21-121-102: Compliance Rate for CF-IQ by Visit (All Domains)
Full Analysis Set

Domain: Social Activity

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline	196 (97.03)	191 (97.45)
Week 4	193 (95.54)	194 (98.98)
Absolute Change at Week 4	187 (92.57)	189 (96.43)
Week 24	195 (96.53)	183 (93.37)
Absolute Change at Week 24	190 (94.06)	179 (91.33)
Week 52	188 (93.07)	181 (92.35)
Absolute Change at Week 52	182 (90.10)	176 (89.80)
Through Week 52	197 (97.52)	190 (96.94)
Absolute Change through Week 52	191 (94.55)	185 (94.39)

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

Table 1.2.1.13.1.1
Study VX21-121-102: Compliance Rate for CF-IQ by Visit (All Domains)
Full Analysis Set

Domain: Emotional

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline	196 (97.03)	191 (97.45)
Week 4	194 (96.04)	195 (99.49)
Absolute Change at Week 4	188 (93.07)	190 (96.94)
Week 24	195 (96.53)	184 (93.88)
Absolute Change at Week 24	190 (94.06)	180 (91.84)
Week 52	188 (93.07)	181 (92.35)
Absolute Change at Week 52	182 (90.10)	176 (89.80)
Through Week 52	197 (97.52)	190 (96.94)
Absolute Change through Week 52	191 (94.55)	185 (94.39)

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

Table 1.2.1.13.1.1
Study VX21-121-102: Compliance Rate for CF-IQ by Visit (All Domains)
Full Analysis Set

Domain: Work/School Limitation

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline	196 (97.03)	190 (96.94)
Week 4	193 (95.54)	194 (98.98)
Absolute Change at Week 4	187 (92.57)	188 (95.92)
Week 24	195 (96.53)	183 (93.37)
Absolute Change at Week 24	190 (94.06)	179 (91.33)
Week 52	188 (93.07)	181 (92.35)
Absolute Change at Week 52	182 (90.10)	175 (89.29)
Through Week 52	197 (97.52)	190 (96.94)
Absolute Change through Week 52	191 (94.55)	184 (93.88)

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

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

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
ppFEV$_1$ at baseline <70 %

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
ppFEV$_1$ at baseline <70 %

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
ppFEV$_1$ at baseline ≥70 %

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
ppFEV$_1$ at baseline ≥70 %

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Age at screening <18 years

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Age at screening <18 years

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Age at screening ≥18 years

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Age at screening ≥18 years

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
SwCl at baseline <30 mmol/L

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
SwCl at baseline <30 mmol/L

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

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

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Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
SwCl at baseline ≥30 mmol/L

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
SwCl at baseline ≥30 mmol/L

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Sex = Male

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Sex = Male

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Sex = Female

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Sex = Female

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Region = North America

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Region = North America

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Region = Rest of World

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

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

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Region = Rest of World

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

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

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

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

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

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

$ppFEV_1$ at baseline <70 %

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

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

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

$ppFEV_1$ at baseline <70 %

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

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

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

$ppFEV_1$ at baseline ≥70 %

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

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

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

$ppFEV_1$ at baseline ≥70 %

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

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

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

Age at screening <18 years

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

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

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

Age at screening <18 years

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

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

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

Age at screening ≥18 years

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

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

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

Age at screening ≥18 years

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

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

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

SwCl at baseline <30 mmol/L

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

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

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

SwCl at baseline <30 mmol/L

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

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

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

SwCl at baseline ≥30 mmol/L

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

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

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

SwCl at baseline ≥30 mmol/L

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

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

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

Sex = Male

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

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

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

Sex = Male

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

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

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

Sex = Female

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

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

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

Sex = Female

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

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

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

Region = North America

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

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

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

Region = North America

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

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

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

Region = Rest of World

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

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

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

Region = Rest of World

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

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

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

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

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

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

ppFEV$_1$ at baseline <70 %

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

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

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

ppFEV$_1$ at baseline <70 %

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

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

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

ppFEV$_1$ at baseline ≥70 %

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

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

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

ppFEV$_1$ at baseline ≥70 %

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

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

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

SwCl at baseline <30 mmol/L

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

Subgroup criteria are not met for this subgroup factor.

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

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

SwCl at baseline ≥30 mmol/L

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

Subgroup criteria are not met for this subgroup factor.

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

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

Sex = Male

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

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

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

Sex = Male

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

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

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

Sex = Female

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

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

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

Sex = Female

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

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

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

Region = North America

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

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

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

Region = North America

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

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

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

Region = Rest of World

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

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

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

Region = Rest of World

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

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

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

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

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

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

ppFEV$_1$ at baseline <70 %

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

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

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

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.72 (-11.43, -6.01)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-0.88 (0.14)
Hedges' 95% CI		(-1.16, -0.59)
Hedges' P-value		<0.0001

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

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

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	86	92
mean (SD)	54.49 (17.65)	54.66 (16.55)
Week 52		
n	78	82
mean (SD)	52.79 (19.08)	48.73 (22.70)
Absolute Change at Week 52		
n	77	82
mean (SD)	-1.37 (14.27)	-6.91 (14.11)
Absolute Change through Week 52 (MMRM)		
n	83	90
LS mean (SE)	0.28 (0.96)	-7.26 (0.93)
95% CI of LS mean	(-1.62, 2.18)	(-9.10, -5.43)
P-value within Treatment	0.7696	<0.0001

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

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

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.55 (-10.19, -4.90)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-0.85 (0.16)
Hedges' 95% CI		(-1.17, -0.54)
Hedges' P-value		<0.0001

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

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

Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	31	26
mean (SD)	50.43 (13.77)	54.83 (16.58)
Week 52		
n	26	22
mean (SD)	53.69 (19.56)	51.14 (24.87)
Absolute Change at Week 52		
n	26	22
mean (SD)	2.79 (16.77)	-5.90 (15.76)
Absolute Change through Week 52 (MMRM)		
n	29	24
LS mean (SE)	2.03 (2.06)	-5.79 (2.27)
95% CI of LS mean	(-2.10, 6.16)	(-10.34, -1.24)
P-value within Treatment	0.3275	0.0137

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

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

Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.82 (-13.99, -1.65)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0140
Hedges' G (SE)		-0.70 (0.28)
Hedges' 95% CI		(-1.26, -0.13)
Hedges' P-value		0.0164

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

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

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	170	168
mean (SD)	54.98 (18.86)	53.35 (17.16)
Week 52		
n	160	149
mean (SD)	53.39 (18.78)	45.86 (20.14)
Absolute Change at Week 52		
n	159	148
mean (SD)	-1.59 (10.98)	-8.58 (12.10)
Absolute Change through Week 52 (MMRM)		
n	166	164
LS mean (SE)	0.22 (0.70)	-7.74 (0.71)
95% CI of LS mean	(-1.16, 1.60)	(-9.15, -6.34)
P-value within Treatment	0.7568	<0.0001

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

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

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.96 (-9.93, -5.99)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-0.87 (0.11)
Hedges' 95% CI		(-1.10, -0.65)
Hedges' P-value		<0.0001

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

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

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	17
mean (SD)	23.78 (6.24)	24.96 (2.17)
Week 52		
n	16	12
mean (SD)	24.53 (7.90)	23.21 (7.27)
Absolute Change at Week 52		
n	16	12
mean (SD)	0.23 (5.81)	-1.67 (6.87)
Absolute Change through Week 52 (MMRM)		
n	18	16
LS mean (SE)	7.82 (2.09)	-1.71 (2.25)
95% CI of LS mean	(3.54, 12.11)	(-6.31, 2.89)
P-value within Treatment	0.0008	0.4526

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

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

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.53 (-15.88, -3.19)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0046
Hedges' G (SE)		-1.04 (0.36)
Hedges' 95% CI		(-1.77, -0.31)
Hedges' P-value		0.0066

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

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

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	182	177
mean (SD)	57.46 (15.97)	56.30 (15.22)
Week 52		
n	169	158
mean (SD)	56.28 (17.17)	48.29 (20.50)
Absolute Change at Week 52		
n	169	158
mean (SD)	-1.09 (12.43)	-8.74 (12.82)
Absolute Change through Week 52 (MMRM)		
n	177	172
LS mean (SE)	-0.17 (0.70)	-8.07 (0.72)
95% CI of LS mean	(-1.55, 1.21)	(-9.48, -6.66)
P-value within Treatment	0.8087	<0.0001

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

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

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.90 (-9.88, -5.92)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-0.84 (0.11)
Hedges' 95% CI		(-1.06, -0.62)
Hedges' P-value		<0.0001

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

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

Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	119	116
mean (SD)	57.27 (17.13)	54.20 (16.36)
Week 52		
n	112	105
mean (SD)	56.98 (17.51)	47.49 (20.16)
Absolute Change at Week 52		
n	112	105
mean (SD)	-0.13 (12.79)	-8.03 (12.79)
Absolute Change through Week 52 (MMRM)		
n	115	115
LS mean (SE)	0.63 (0.90)	-6.75 (0.91)
95% CI of LS mean	(-1.15, 2.41)	(-8.54, -4.96)
P-value within Treatment	0.4848	<0.0001

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

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

Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.38 (-9.91, -4.85)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-0.76 (0.14)
Hedges' 95% CI		(-1.03, -0.49)
Hedges' P-value		<0.0001

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

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

Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	82	78
mean (SD)	49.92 (18.96)	52.59 (18.08)
Week 52		
n	74	66
mean (SD)	48.05 (19.60)	45.02 (21.86)
Absolute Change at Week 52		
n	73	65
mean (SD)	-2.27 (10.63)	-8.58 (12.42)
Absolute Change through Week 52 (MMRM)		
n	80	73
LS mean (SE)	0.49 (0.99)	-8.83 (1.05)
95% CI of LS mean	(-1.47, 2.44)	(-10.92, -6.75)
P-value within Treatment	0.6243	<0.0001

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

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

Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.32 (-12.18, -6.45)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-1.04 (0.17)
Hedges' 95% CI		(-1.38, -0.70)
Hedges' P-value		<0.0001

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

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

Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	90	85
mean (SD)	57.05 (16.97)	55.27 (17.04)
Week 52		
n	86	73
mean (SD)	57.67 (18.13)	49.05 (20.49)
Absolute Change at Week 52		
n	85	72
mean (SD)	1.01 (12.42)	-8.68 (10.96)
Absolute Change through Week 52 (MMRM)		
n	89	85
LS mean (SE)	0.76 (0.88)	-9.03 (0.92)
95% CI of LS mean	(-0.98, 2.50)	(-10.84, -7.21)
P-value within Treatment	0.3889	<0.0001

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

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

Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.79 (-12.30, -7.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-1.16 (0.16)
Hedges' 95% CI		(-1.48, -0.84)
Hedges' P-value		<0.0001

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

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

Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	111	109
mean (SD)	52.02 (18.94)	52.21 (17.01)
Week 52		
n	100	98
mean (SD)	49.79 (18.75)	44.66 (20.94)
Absolute Change at Week 52		
n	100	98
mean (SD)	-2.66 (11.43)	-7.91 (13.75)
Absolute Change through Week 52 (MMRM)		
n	106	103
LS mean (SE)	0.32 (0.98)	-6.26 (1.00)
95% CI of LS mean	(-1.62, 2.26)	(-8.23, -4.29)
P-value within Treatment	0.7468	<0.0001

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

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

Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.58 (-9.34, -3.81)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-0.65 (0.14)
Hedges' 95% CI		(-0.93, -0.37)
Hedges' P-value		<0.0001

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

Table 1.2.2.4.2.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1930*
Age at screening (<18 years vs. ≥18 years) [2]	0.8045*
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.5013
Sex (Male vs. Female) [1]	0.4966*
Region (North America vs. Rest of the World) [1]	0.6613*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at Baseline <70%

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Non-missing value at Week 52, N1	107	86
Number of subjects with missing value at Week 52	7	15
SwCl <30 mmol/L at Week 52, n (%)	60 (52.63)	68 (67.33)
Relative Risk (RR) (95% CI)		1.2685 (1.0363, 1.5528)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0211*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at Baseline ≥70%

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Non-missing value at Week 52, N1	78	82
Number of subjects with missing value at Week 52	9	10
SwCl <30 mmol/L at Week 52, n (%)	57 (65.52)	62 (67.39)
Relative Risk (RR) (95% CI)		1.0335 (0.8492, 1.2577)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7426*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Age at Screening < 18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Non-missing value at Week 52, N1	26	22
Number of subjects with missing value at Week 52	5	4
SwCl <30 mmol/L at Week 52, n (%)	18 (58.06)	16 (61.54)
Relative Risk (RR) (95% CI)		1.0968 (0.7092, 1.6963)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6778

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Age at Screening ≥ 18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Non-missing value at Week 52, N1	160	149
Number of subjects with missing value at Week 52	11	21
SwCl <30 mmol/L at Week 52, n (%)	99 (57.89)	116 (68.24)
Relative Risk (RR) (95% CI)		1.1629 (1.0012, 1.3506)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0482*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Non-missing value at Week 52, N1	16	12
Number of subjects with missing value at Week 52	3	5
SwCl <30 mmol/L at Week 52, n (%)	16 (84.21)	12 (70.59)
Relative Risk (RR) (95% CI)		0.7455 (0.5239, 1.0607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1026*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Non-missing value at Week 52, N1	169	158
Number of subjects with missing value at Week 52	13	19
SwCl <30 mmol/L at Week 52, n (%)	100 (54.95)	119 (67.23)
Relative Risk (RR) (95% CI)		1.1157 (0.9825, 1.2668)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0913

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Non-missing value at Week 52, N1	112	105
Number of subjects with missing value at Week 52	7	11
SwCl <30 mmol/L at Week 52, n (%)	64 (53.78)	80 (68.97)
Relative Risk (RR) (95% CI)		1.1129 (0.9112, 1.3593)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2943

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Non-missing value at Week 52, N1	74	66
Number of subjects with missing value at Week 52	9	14
SwCl <30 mmol/L at Week 52, n (%)	53 (63.86)	52 (65.00)
Relative Risk (RR) (95% CI)		1.0880 (0.8813, 1.3433)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4328*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Non-missing value at Week 52, N1	86	73
Number of subjects with missing value at Week 52	5	14
SwCl <30 mmol/L at Week 52, n (%)	48 (52.75)	52 (59.77)
Relative Risk (RR) (95% CI)		1.1035 (0.8662, 1.4058)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4254*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Non-missing value at Week 52, N1	100	98
Number of subjects with missing value at Week 52	11	11
SwCl <30 mmol/L at Week 52, n (%)	69 (62.16)	80 (73.39)
Relative Risk (RR) (95% CI)		1.1809 (0.9954, 1.4010)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0565*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.8520*
Age at screening (<18 years vs. ≥18 years) [2]	0.3259*
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.0562*
Sex (Male vs. Female) [1]	0.5638*
Region (North America vs. Rest of the World) [1]	0.2015*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.
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Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline <70%

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Non-missing value at Week 52, N1	107	86
Number of subjects with missing value at Week 52	7	15
SwCl <30 mmol/L at Week 52, n (%)	15 (13.16)	24 (23.76)
Relative Risk (RR) (95% CI)		2.1099 (1.2915, 3.4470)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0029*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline ≥70%

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Non-missing value at Week 52, N1	78	82
Number of subjects with missing value at Week 52	9	10
SwCl <30 mmol/L at Week 52, n (%)	10 (11.49)	17 (18.48)
Relative Risk (RR) (95% CI)		1.8813 (0.9901, 3.5746)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0536*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

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Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Age at Screening < 18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Non-missing value at Week 52, N1	26	22
Number of subjects with missing value at Week 52	5	4
SwCl <30 mmol/L at Week 52, n (%)	5 (16.13)	4 (15.38)
Relative Risk (RR) (95% CI)		1.3516 (0.4579, 3.9897)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.5854*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Age at Screening ≥ 18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Non-missing value at Week 52, N1	160	149
Number of subjects with missing value at Week 52	11	21
SwCl <30 mmol/L at Week 52, n (%)	20 (11.70)	37 (21.76)
Relative Risk (RR) (95% CI)		2.1451 (1.4042, 3.2769)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0004*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

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Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Non-missing value at Week 52, N1	16	12
Number of subjects with missing value at Week 52	3	5
SwCl <30 mmol/L at Week 52, n (%)	13 (68.42)	10 (58.82)
Relative Risk (RR) (95% CI)		0.9255 (0.5760, 1.4869)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7488

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Non-missing value at Week 52, N1	169	158
Number of subjects with missing value at Week 52	13	19
SwCl <30 mmol/L at Week 52, n (%)	12 (6.59)	31 (17.51)
Relative Risk (RR) (95% CI)		2.7920 (1.5863, 4.9142)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0004*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Non-missing value at Week 52, N1	112	105
Number of subjects with missing value at Week 52	7	11
SwCl <30 mmol/L at Week 52, n (%)	9 (7.56)	22 (18.97)
Relative Risk (RR) (95% CI)		2.3565 (1.2977, 4.2792)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0049*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

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Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Non-missing value at Week 52, N1	74	66
Number of subjects with missing value at Week 52	9	14
SwCl <30 mmol/L at Week 52, n (%)	16 (19.28)	19 (23.75)
Relative Risk (RR) (95% CI)		1.6772 (1.0117, 2.7803)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0449*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Non-missing value at Week 52, N1	86	73
Number of subjects with missing value at Week 52	5	14
SwCl <30 mmol/L at Week 52, n (%)	5 (5.49)	15 (17.24)
Relative Risk (RR) (95% CI)		2.9524 (1.4412, 6.0483)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0031*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Non-missing value at Week 52, N1	100	98
Number of subjects with missing value at Week 52	11	11
SwCl <30 mmol/L at Week 52, n (%)	20 (18.02)	26 (23.85)
Relative Risk (RR) (95% CI)		1.6460 (1.0479, 2.5854)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0305*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

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Table 1.2.2.5.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.9737
Age at screening (<18 years vs. ≥18 years) [2]	0.5553
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.8257
Sex (Male vs. Female) [1]	0.8473
Region (North America vs. Rest of the World) [1]	0.4315

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	114	100
mean (SD)	64.31 (12.83)	66.55 (13.57)
Week 52		
n	111	93
mean (SD)	64.86 (12.99)	67.76 (13.21)
Absolute Change at Week 52		
n	111	93
mean (SD)	0.35 (3.64)	0.55 (3.10)
Absolute Change at Week 52 (MMRM)		
n	111	92
LS mean (SE)	0.31 (0.32)	0.44 (0.35)
95% CI of LS mean	(-0.31, 0.94)	(-0.24, 1.12)
P-value within Treatment	0.3252	0.2026

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-0.80, 1.05)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7842
Hedges' G (SE)		0.04 (0.14)
Hedges' 95% CI		(-0.24, 0.32)
Hedges' P-value		0.7844

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

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Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	87	92
mean (SD)	64.90 (15.00)	63.68 (13.08)
Week 52		
n	77	87
mean (SD)	66.22 (14.12)	65.42 (12.33)
Absolute Change at Week 52		
n	77	87
mean (SD)	0.74 (4.74)	1.56 (4.25)
Absolute Change at Week 52 (MMRM)		
n	76	87
LS mean (SE)	0.77 (0.49)	1.65 (0.47)
95% CI of LS mean	(-0.20, 1.75)	(0.72, 2.58)
P-value within Treatment	0.1195	0.0006

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.87 (-0.47, 2.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2022
Hedges' G (SE)		0.20 (0.16)
Hedges' 95% CI		(-0.11, 0.51)
Hedges' P-value		0.2039

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	31	26
mean (SD)	52.79 (13.27)	52.30 (10.26)
Week 52		
n	27	25
mean (SD)	55.90 (11.49)	56.60 (8.21)
Absolute Change at Week 52		
n	27	25
mean (SD)	2.82 (5.45)	4.64 (4.01)
Absolute Change at Week 52 (MMRM)		
n	27	24
LS mean (SE)	2.47 (0.93)	4.61 (1.01)
95% CI of LS mean	(0.60, 4.34)	(2.57, 6.65)
P-value within Treatment	0.0106	<0.0001

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.14 (-0.62, 4.91)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1260
Hedges' G (SE)		0.43 (0.28)
Hedges' 95% CI		(-0.13, 0.99)
Hedges' P-value		0.1298

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	171	169
mean (SD)	66.67 (12.75)	67.05 (12.65)
Week 52		
n	162	158
mean (SD)	66.98 (13.08)	68.09 (12.66)
Absolute Change at Week 52		
n	162	158
mean (SD)	0.13 (3.72)	0.46 (3.34)
Absolute Change at Week 52 (MMRM)		
n	160	155
LS mean (SE)	0.16 (0.28)	0.46 (0.28)
95% CI of LS mean	(-0.38, 0.71)	(-0.10, 1.01)
P-value within Treatment	0.5542	0.1047

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.29 (-0.48, 1.07)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4569
Hedges' G (SE)		0.08 (0.11)
Hedges' 95% CI		(-0.14, 0.31)
Hedges' P-value		0.4571

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	17
mean (SD)	58.59 (12.74)	65.53 (8.06)
Week 52		
n	17	14
mean (SD)	60.35 (14.93)	69.02 (10.01)
Absolute Change at Week 52		
n	17	14
mean (SD)	1.05 (4.76)	2.45 (4.28)
Absolute Change at Week 52 (MMRM)		
n	17	13
LS mean (SE)	0.95 (1.02)	2.62 (1.13)
95% CI of LS mean	(-1.12, 3.02)	(0.32, 4.92)
P-value within Treatment	0.3556	0.0271

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.66 (-1.44, 4.76)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2824
Hedges' G (SE)		0.39 (0.36)
Hedges' 95% CI		(-0.35, 1.13)
Hedges' P-value		0.2894

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	182	176
mean (SD)	64.91 (13.36)	65.17 (13.73)
Week 52		
n	171	168
mean (SD)	65.68 (12.93)	66.34 (13.00)
Absolute Change at Week 52		
n	171	168
mean (SD)	0.50 (4.02)	0.91 (3.67)
Absolute Change at Week 52 (MMRM)		
n	170	166
LS mean (SE)	0.45 (0.29)	0.88 (0.30)
95% CI of LS mean	(-0.12, 1.03)	(0.29, 1.46)
P-value within Treatment	0.1209	0.0033

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.42 (-0.40, 1.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3093
Hedges' G (SE)		0.11 (0.11)
Hedges' 95% CI		(-0.10, 0.33)
Hedges' P-value		0.3096

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	119	115
mean (SD)	69.01 (13.62)	69.99 (14.06)
Week 52		
n	111	110
mean (SD)	69.83 (13.13)	71.26 (12.81)
Absolute Change at Week 52		
n	111	110
mean (SD)	0.34 (4.13)	0.72 (3.78)
Absolute Change at Week 52 (MMRM)		
n	110	110
LS mean (SE)	0.34 (0.37)	0.69 (0.37)
95% CI of LS mean	(-0.38, 1.07)	(-0.04, 1.42)
P-value within Treatment	0.3489	0.0635

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.34 (-0.68, 1.37)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5104
Hedges' G (SE)		0.09 (0.13)
Hedges' 95% CI		(-0.18, 0.35)
Hedges' P-value		0.5104

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	80
mean (SD)	58.14 (11.22)	58.03 (8.05)
Week 52		
n	78	73
mean (SD)	59.09 (11.16)	59.37 (8.78)
Absolute Change at Week 52		
n	78	73
mean (SD)	0.75 (4.10)	1.51 (3.60)
Absolute Change at Week 52 (MMRM)		
n	77	69
LS mean (SE)	0.68 (0.44)	1.52 (0.47)
95% CI of LS mean	(-0.20, 1.55)	(0.59, 2.44)
P-value within Treatment	0.1296	0.0015

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.84 (-0.44, 2.11)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1956
Hedges' G (SE)		0.21 (0.17)
Hedges' 95% CI		(-0.11, 0.54)
Hedges' P-value		0.1968

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	91	87
mean (SD)	65.11 (15.37)	66.99 (13.97)
Week 52		
n	89	78
mean (SD)	64.99 (14.46)	68.05 (13.51)
Absolute Change at Week 52		
n	89	78
mean (SD)	-0.19 (4.21)	0.04 (3.12)
Absolute Change at Week 52 (MMRM)		
n	88	77
LS mean (SE)	-0.08 (0.39)	-0.07 (0.41)
95% CI of LS mean	(-0.85, 0.69)	(-0.88, 0.73)
P-value within Treatment	0.8439	0.8620

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-1.11, 1.12)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9918
Hedges' G (SE)		0.00 (0.16)
Hedges' 95% CI		(-0.31, 0.31)
Hedges' P-value		0.9918

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	111	108
mean (SD)	64.08 (12.31)	63.55 (12.62)
Week 52		
n	100	105
mean (SD)	65.76 (12.47)	65.38 (12.12)
Absolute Change at Week 52		
n	100	105
mean (SD)	1.13 (3.94)	1.77 (3.96)
Absolute Change at Week 52 (MMRM)		
n	99	102
LS mean (SE)	1.02 (0.39)	1.85 (0.39)
95% CI of LS mean	(0.26, 1.79)	(1.08, 2.62)
P-value within Treatment	0.0091	<0.0001

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

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.83 (-0.26, 1.91)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1334
Hedges' G (SE)		0.21 (0.14)
Hedges' 95% CI		(-0.07, 0.49)
Hedges' P-value		0.1346

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

Table 1.2.2.6.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Time-to-First Pulmonary Exacerbation through Week 52
Full Analysis Set

Subgroup	P-value for Interaction based on Hazard Ratio
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.9963
Age at screening (<18 years vs. ≥18 years) [2]	0.3480
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.0951
Sex (Male vs. Female) [1]	0.4719
Region (North America vs. Rest of the World) [1]	0.8818

-Subgroup Criteria (SC): subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
-P-values are reported for each subgroup factor only when SC are fulfilled. If not, display '-'.
- [1] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$ and baseline sweat chloride, and age at screening (<18 vs ≥18 years).
- [2] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$ and baseline sweat chloride.
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Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at Baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	41 (35.96)	32 (31.68)
Subjects Censored	73 (64.04)	69 (68.32)
Event-free time (weeks)		
75 percent subjects	24.4286	27.7143
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9737 (0.9206, 0.9914)	0.9901 (0.9318, 0.9986)
4 Weeks	0.9474 (0.8866, 0.9760)	0.9802 (0.9231, 0.9950)
8 Weeks	0.9120 (0.8425, 0.9516)	0.9304 (0.8595, 0.9662)
12 Weeks	0.8677 (0.7901, 0.9180)	0.9004 (0.8227, 0.9451)
16 Weeks	0.8323 (0.7497, 0.8896)	0.8604 (0.7756, 0.9148)
24 Weeks	0.7614 (0.6717, 0.8297)	0.7703 (0.6749, 0.8410)
36 Weeks	0.6905 (0.5964, 0.7669)	0.7095 (0.6096, 0.7882)
52 Weeks	0.6367 (0.5407, 0.7179)	0.6777 (0.5759, 0.7601)
Hazard Ratio (95% CI)*	-	0.8410 (0.5274, 1.3412)
Two-sided P-value, superiority*	-	0.4672

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at Baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	19 (21.84)	18 (19.57)
Subjects Censored	68 (78.16)	74 (80.43)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9885 (0.9212, 0.9984)	0.9891 (0.9253, 0.9985)
4 Weeks	0.9885 (0.9212, 0.9984)	0.9783 (0.9159, 0.9945)
8 Weeks	0.9652 (0.8961, 0.9887)	0.9457 (0.8744, 0.9770)
12 Weeks	0.9420 (0.8662, 0.9754)	0.9239 (0.8470, 0.9630)
16 Weeks	0.9181 (0.8359, 0.9601)	0.9022 (0.8204, 0.9479)
24 Weeks	0.8943 (0.8067, 0.9436)	0.8689 (0.7807, 0.9233)
36 Weeks	0.8105 (0.7093, 0.8794)	0.8466 (0.7547, 0.9062)
52 Weeks	0.7705 (0.6635, 0.8473)	0.8021 (0.7043, 0.8704)
Hazard Ratio (95% CI)*	-	0.8557 (0.4483, 1.6331)
Two-sided P-value, superiority*	-	0.6365

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	6 (19.35)	2 (7.69)
Subjects Censored	25 (80.65)	24 (92.31)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	0.9615 (0.7569, 0.9945)
12 Weeks	1.0000 (-, -)	0.9615 (0.7569, 0.9945)
16 Weeks	1.0000 (-, -)	0.9615 (0.7569, 0.9945)
24 Weeks	0.9310 (0.7514, 0.9823)	0.9215 (0.7208, 0.9798)
36 Weeks	0.8607 (0.6701, 0.9453)	0.9215 (0.7208, 0.9798)
52 Weeks	0.7873 (0.5861, 0.8985)	0.9215 (0.7208, 0.9798)
Hazard Ratio (95% CI)*	-	0.3827 (0.0752, 1.9486)
Two-sided P-value, superiority*	-	0.2474

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	54 (31.58)	48 (28.24)
Subjects Censored	117 (68.42)	122 (71.76)
Event-free time (weeks)		
75 percent subjects	27.1429	37.7143
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9766 (0.9389, 0.9912)	0.9882 (0.9538, 0.9970)
4 Weeks	0.9591 (0.9161, 0.9803)	0.9765 (0.9385, 0.9911)
8 Weeks	0.9238 (0.8723, 0.9550)	0.9351 (0.8860, 0.9636)
12 Weeks	0.8825 (0.8238, 0.9225)	0.9056 (0.8505, 0.9410)
16 Weeks	0.8469 (0.7834, 0.8931)	0.8700 (0.8094, 0.9124)
24 Weeks	0.7995 (0.7310, 0.8524)	0.8045 (0.7363, 0.8568)
36 Weeks	0.7224 (0.6483, 0.7835)	0.7563 (0.6841, 0.8143)
52 Weeks	0.6803 (0.6041, 0.7449)	0.7133 (0.6383, 0.7756)
Hazard Ratio (95% CI)*	-	0.8842 (0.5989, 1.3054)
Two-sided P-value, superiority*	-	0.5358

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	7 (36.84)	2 (11.76)
Subjects Censored	12 (63.16)	15 (88.24)
Event-free time (weeks)		
75 percent subjects	18.2857	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
4 Weeks	0.8947 (0.6408, 0.9726)	1.0000 (-, -)
8 Weeks	0.8947 (0.6408, 0.9726)	1.0000 (-, -)
12 Weeks	0.7895 (0.5319, 0.9153)	1.0000 (-, -)
16 Weeks	0.7895 (0.5319, 0.9153)	1.0000 (-, -)
24 Weeks	0.6842 (0.4279, 0.8439)	0.9412 (0.6502, 0.9915)
36 Weeks	0.6842 (0.4279, 0.8439)	0.8824 (0.6060, 0.9692)
52 Weeks	0.6272 (0.3725, 0.8022)	0.8824 (0.6060, 0.9692)
Hazard Ratio (95% CI)*	-	0.1796 (0.0272, 1.1873)
Two-sided P-value, superiority*	-	0.0748

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	53 (29.12)	48 (27.12)
Subjects Censored	129 (70.88)	129 (72.88)
Event-free time (weeks)		
75 percent subjects	36.1429	38.7143
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9835 (0.9498, 0.9947)	0.9887 (0.9556, 0.9972)
4 Weeks	0.9725 (0.9351, 0.9884)	0.9774 (0.9409, 0.9915)
8 Weeks	0.9391 (0.8928, 0.9658)	0.9320 (0.8834, 0.9608)
12 Weeks	0.9113 (0.8592, 0.9447)	0.9036 (0.8495, 0.9390)
16 Weeks	0.8775 (0.8199, 0.9176)	0.8694 (0.8101, 0.9113)
24 Weeks	0.8325 (0.7693, 0.8798)	0.8061 (0.7395, 0.8574)
36 Weeks	0.7480 (0.6775, 0.8053)	0.7656 (0.6955, 0.8216)
52 Weeks	0.7011 (0.6276, 0.7628)	0.7250 (0.6522, 0.7851)
Hazard Ratio (95% CI)*	-	0.9320 (0.6304, 1.3778)
Two-sided P-value, superiority*	-	0.7239

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	29 (24.37)	29 (25.00)
Subjects Censored	90 (75.63)	87 (75.00)
Event-free time (weeks)		
75 percent subjects	51.7143	40.1429
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9916 (0.9419, 0.9988)	0.9914 (0.9404, 0.9988)
4 Weeks	0.9831 (0.9342, 0.9958)	0.9741 (0.9220, 0.9916)
8 Weeks	0.9404 (0.8790, 0.9711)	0.9483 (0.8885, 0.9764)
12 Weeks	0.9146 (0.8470, 0.9531)	0.9138 (0.8457, 0.9527)
16 Weeks	0.8887 (0.8160, 0.9338)	0.8791 (0.8045, 0.9266)
24 Weeks	0.8542 (0.7759, 0.9067)	0.8008 (0.7156, 0.8629)
36 Weeks	0.8022 (0.7175, 0.8639)	0.7745 (0.6868, 0.8405)
52 Weeks	0.7477 (0.6574, 0.8175)	0.7481 (0.6582, 0.8176)
Hazard Ratio (95% CI)*	-	0.9911 (0.5896, 1.6659)
Two-sided P-value, superiority*	-	0.9730

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	31 (37.35)	21 (26.25)
Subjects Censored	52 (62.65)	59 (73.75)
Event-free time (weeks)		
75 percent subjects	24.7143	42.8571
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9639 (0.8921, 0.9882)	0.9875 (0.9146, 0.9982)
4 Weeks	0.9398 (0.8613, 0.9745)	0.9875 (0.9146, 0.9982)
8 Weeks	0.9277 (0.8462, 0.9669)	0.9245 (0.8396, 0.9654)
12 Weeks	0.8794 (0.7874, 0.9332)	0.9118 (0.8239, 0.9570)
16 Weeks	0.8427 (0.7446, 0.9055)	0.8865 (0.7932, 0.9393)
24 Weeks	0.7694 (0.6626, 0.8463)	0.8480 (0.7478, 0.9107)
36 Weeks	0.6591 (0.5457, 0.7505)	0.7827 (0.6738, 0.8590)
52 Weeks	0.6213 (0.5069, 0.7165)	0.7287 (0.6146, 0.8141)
Hazard Ratio (95% CI)*	-	0.7426 (0.4263, 1.2935)
Two-sided P-value, superiority*	-	0.2932

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	25 (27.47)	21 (24.14)
Subjects Censored	66 (72.53)	66 (75.86)
Event-free time (weeks)		
75 percent subjects	48.1429	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9670 (0.9013, 0.9892)	0.9770 (0.9112, 0.9942)
4 Weeks	0.9670 (0.9013, 0.9892)	0.9770 (0.9112, 0.9942)
8 Weeks	0.9226 (0.8444, 0.9623)	0.9310 (0.8529, 0.9684)
12 Weeks	0.9003 (0.8172, 0.9469)	0.9080 (0.8245, 0.9529)
16 Weeks	0.8781 (0.7907, 0.9306)	0.8966 (0.8106, 0.9448)
24 Weeks	0.8559 (0.7648, 0.9137)	0.8150 (0.7159, 0.8824)
36 Weeks	0.7892 (0.6896, 0.8600)	0.7909 (0.6887, 0.8628)
52 Weeks	0.7190 (0.6127, 0.8008)	0.7538 (0.6476, 0.8321)
Hazard Ratio (95% CI)*	-	0.8874 (0.4955, 1.5895)
Two-sided P-value, superiority*	-	0.6880

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	35 (31.53)	29 (26.61)
Subjects Censored	76 (68.47)	80 (73.39)
Event-free time (weeks)		
75 percent subjects	26.1429	38.7143
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9910 (0.9378, 0.9987)	1.0000 (-, -)
4 Weeks	0.9640 (0.9068, 0.9863)	0.9817 (0.9286, 0.9954)
8 Weeks	0.9458 (0.8833, 0.9753)	0.9449 (0.8814, 0.9748)
12 Weeks	0.8998 (0.8263, 0.9432)	0.9171 (0.8467, 0.9560)
16 Weeks	0.8627 (0.7825, 0.9148)	0.8706 (0.7912, 0.9212)
24 Weeks	0.7884 (0.6990, 0.8541)	0.8238 (0.7377, 0.8838)
36 Weeks	0.7046 (0.6089, 0.7811)	0.7676 (0.6757, 0.8365)
52 Weeks	0.6758 (0.5785, 0.7553)	0.7301 (0.6355, 0.8040)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Hazard Ratio (95% CI)*	-	0.8166 (0.4991, 1.3362)
Two-sided P-value, superiority*	-	0.4200

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Time-to-First Pulmonary Exacerbation Requiring Hospitalizatio through Week 52
Full Analysis Set

Subgroup	P-value for Interaction based on Hazard Ratio
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.3324
Age at screening (<18 years vs. ≥18 years) [2]	0.9400
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.9903
Sex (Male vs. Female) [1]	0.4584
Region (North America vs. Rest of the World) [1]	0.9452

- Subgroup Criteria (SC): subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when SC are fulfilled. If not, display '-'.
- [1] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$ and baseline sweat chloride, and age at screening (<18 vs ≥18 years).
- [2] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$ and baseline sweat chloride.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

ppFEV$_1$ at Baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	11 (9.65)	3 (2.97)
Subjects Censored	103 (90.35)	98 (97.03)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9825 (0.9317, 0.9956)	0.9901 (0.9318, 0.9986)
4 Weeks	0.9825 (0.9317, 0.9956)	0.9901 (0.9318, 0.9986)
8 Weeks	0.9825 (0.9317, 0.9956)	0.9901 (0.9318, 0.9986)
12 Weeks	0.9648 (0.9088, 0.9866)	0.9901 (0.9318, 0.9986)
16 Weeks	0.9648 (0.9088, 0.9866)	0.9901 (0.9318, 0.9986)
24 Weeks	0.9559 (0.8973, 0.9814)	0.9801 (0.9228, 0.9950)
36 Weeks	0.9293 (0.8635, 0.9640)	0.9697 (0.9089, 0.9901)
52 Weeks	0.9024 (0.8306, 0.9447)	0.9697 (0.9089, 0.9901)
Hazard Ratio (95% CI)*	-	0.3184 (0.0884, 1.1469)
Two-sided P-value, superiority*	-	0.0801

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

ppFEV$_1$ at Baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	6 (6.90)	5 (5.43)
Subjects Censored	81 (93.10)	87 (94.57)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	0.9884 (0.9203, 0.9984)	0.9891 (0.9253, 0.9985)
12 Weeks	0.9884 (0.9203, 0.9984)	0.9783 (0.9159, 0.9945)
16 Weeks	0.9646 (0.8941, 0.9884)	0.9783 (0.9159, 0.9945)
24 Weeks	0.9646 (0.8941, 0.9884)	0.9673 (0.9020, 0.9893)
36 Weeks	0.9287 (0.8481, 0.9673)	0.9562 (0.8874, 0.9833)
52 Weeks	0.9287 (0.8481, 0.9673)	0.9450 (0.8730, 0.9767)
Hazard Ratio (95% CI)*	-	0.6994 (0.2099, 2.3302)
Two-sided P-value, superiority*	-	0.5603

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	2 (6.45)	1 (3.85)
Subjects Censored	29 (93.55)	25 (96.15)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	1.0000 (-, -)
12 Weeks	1.0000 (-, -)	1.0000 (-, -)
16 Weeks	1.0000 (-, -)	1.0000 (-, -)
24 Weeks	1.0000 (-, -)	1.0000 (-, -)
36 Weeks	0.9643 (0.7724, 0.9949)	1.0000 (-, -)
52 Weeks	0.9286 (0.7435, 0.9816)	0.9600 (0.7484, 0.9943)
Hazard Ratio (95% CI)*	-	0.3035 (0.0187, 4.9211)
Two-sided P-value, superiority*	-	0.4015

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	15 (8.77)	7 (4.12)
Subjects Censored	156 (91.23)	163 (95.88)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9883 (0.9540, 0.9971)	0.9941 (0.9590, 0.9992)
4 Weeks	0.9883 (0.9540, 0.9971)	0.9941 (0.9590, 0.9992)
8 Weeks	0.9824 (0.9465, 0.9943)	0.9882 (0.9538, 0.9970)
12 Weeks	0.9706 (0.9309, 0.9877)	0.9823 (0.9462, 0.9943)
16 Weeks	0.9588 (0.9155, 0.9801)	0.9823 (0.9462, 0.9943)
24 Weeks	0.9529 (0.9080, 0.9761)	0.9704 (0.9305, 0.9876)
36 Weeks	0.9232 (0.8714, 0.9547)	0.9583 (0.9145, 0.9799)
52 Weeks	0.9111 (0.8569, 0.9455)	0.9583 (0.9145, 0.9799)
Hazard Ratio (95% CI)*	-	0.4783 (0.1948, 1.1744)
Two-sided P-value, superiority*	-	0.1076

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	2 (10.53)	0
Subjects Censored	17 (89.47)	17 (100.00)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
4 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
8 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
12 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
16 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
24 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
36 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
52 Weeks	0.8916 (0.6315, 0.9718)	1.0000 (-, -)
Hazard Ratio (95% CI)*	-	N/C
Two-sided P-value, superiority*	-	0.9976

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	15 (8.24)	8 (4.52)
Subjects Censored	167 (91.76)	169 (95.48)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9945 (0.9616, 0.9992)	0.9944 (0.9606, 0.9992)
4 Weeks	0.9945 (0.9616, 0.9992)	0.9944 (0.9606, 0.9992)
8 Weeks	0.9889 (0.9565, 0.9972)	0.9887 (0.9556, 0.9972)
12 Weeks	0.9778 (0.9419, 0.9916)	0.9830 (0.9483, 0.9945)
16 Weeks	0.9665 (0.9270, 0.9848)	0.9830 (0.9483, 0.9945)
24 Weeks	0.9609 (0.9198, 0.9812)	0.9716 (0.9330, 0.9881)
36 Weeks	0.9271 (0.8777, 0.9570)	0.9599 (0.9178, 0.9807)
52 Weeks	0.9157 (0.8641, 0.9483)	0.9541 (0.9103, 0.9768)
Hazard Ratio (95% CI)*	-	0.5516 (0.2338, 1.3015)
Two-sided P-value, superiority*	-	0.1744

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	6 (5.04)	4 (3.45)
Subjects Censored	113 (94.96)	112 (96.55)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9914 (0.9404, 0.9988)
4 Weeks	1.0000 (-, -)	0.9914 (0.9404, 0.9988)
8 Weeks	1.0000 (-, -)	0.9914 (0.9404, 0.9988)
12 Weeks	0.9914 (0.9404, 0.9988)	0.9828 (0.9328, 0.9957)
16 Weeks	0.9828 (0.9328, 0.9957)	0.9828 (0.9328, 0.9957)
24 Weeks	0.9741 (0.9220, 0.9916)	0.9741 (0.9217, 0.9916)
36 Weeks	0.9567 (0.8992, 0.9818)	0.9652 (0.9099, 0.9868)
52 Weeks	0.9480 (0.8878, 0.9763)	0.9652 (0.9099, 0.9868)
Hazard Ratio (95% CI)*	-	0.7180 (0.2004, 2.5725)
Two-sided P-value, superiority*	-	0.6109

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	11 (13.25)	4 (5.00)
Subjects Censored	72 (86.75)	76 (95.00)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9759 (0.9071, 0.9939)	1.0000 (-, -)
4 Weeks	0.9759 (0.9071, 0.9939)	1.0000 (-, -)
8 Weeks	0.9639 (0.8921, 0.9882)	0.9875 (0.9146, 0.9982)
12 Weeks	0.9518 (0.8767, 0.9816)	0.9875 (0.9146, 0.9982)
16 Weeks	0.9396 (0.8610, 0.9744)	0.9875 (0.9146, 0.9982)
24 Weeks	0.9396 (0.8610, 0.9744)	0.9747 (0.9025, 0.9936)
36 Weeks	0.8906 (0.8003, 0.9415)	0.9615 (0.8853, 0.9874)
52 Weeks	0.8655 (0.7703, 0.9232)	0.9481 (0.8676, 0.9802)
Hazard Ratio (95% CI)*	-	0.3688 (0.1162, 1.1707)
Two-sided P-value, superiority*	-	0.0905

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	11 (12.09)	5 (5.75)
Subjects Censored	80 (87.91)	82 (94.25)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9890 (0.9246, 0.9984)	0.9885 (0.9212, 0.9984)
4 Weeks	0.9890 (0.9246, 0.9984)	0.9885 (0.9212, 0.9984)
8 Weeks	0.9779 (0.9145, 0.9944)	0.9885 (0.9212, 0.9984)
12 Weeks	0.9668 (0.9006, 0.9892)	0.9770 (0.9112, 0.9942)
16 Weeks	0.9557 (0.8862, 0.9831)	0.9770 (0.9112, 0.9942)
24 Weeks	0.9446 (0.8719, 0.9765)	0.9654 (0.8965, 0.9887)
36 Weeks	0.9001 (0.8168, 0.9467)	0.9533 (0.8803, 0.9822)
52 Weeks	0.8777 (0.7901, 0.9304)	0.9409 (0.8638, 0.9750)
Hazard Ratio (95% CI)*	-	0.4779 (0.1658, 1.3774)
Two-sided P-value, superiority*	-	0.1716

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	6 (5.41)	3 (2.75)
Subjects Censored	105 (94.59)	106 (97.25)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9910 (0.9378, 0.9987)	1.0000 (-, -)
4 Weeks	0.9910 (0.9378, 0.9987)	1.0000 (-, -)
8 Weeks	0.9910 (0.9378, 0.9987)	0.9908 (0.9367, 0.9987)
12 Weeks	0.9817 (0.9289, 0.9954)	0.9908 (0.9367, 0.9987)
16 Weeks	0.9725 (0.9171, 0.9910)	0.9908 (0.9367, 0.9987)
24 Weeks	0.9725 (0.9171, 0.9910)	0.9815 (0.9280, 0.9953)
36 Weeks	0.9539 (0.8929, 0.9806)	0.9721 (0.9161, 0.9909)
52 Weeks	0.9444 (0.8804, 0.9746)	0.9721 (0.9161, 0.9909)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Hazard Ratio (95% CI)*	-	0.5036 (0.1258, 2.0161)
Two-sided P-value, superiority*	-	0.3324

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Subgroup	P-value for Interaction based on Hazard Ratio
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.3101
Age at screening (<18 years vs. ≥18 years) [2]	0.7359
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.9888
Sex (Male vs. Female) [1]	0.6524
Region (North America vs. Rest of the World) [1]	0.9544

- Subgroup Criteria (SC): subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when SC are fulfilled. If not, display '-'.
- [1] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$ and baseline sweat chloride, and age at screening (<18 vs ≥18 years).
- [2] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$ and baseline sweat chloride.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

ppFEV$_1$ at Baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	19 (16.67)	5 (4.95)
Subjects Censored	95 (83.33)	96 (95.05)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9825 (0.9317, 0.9956)	0.9901 (0.9318, 0.9986)
4 Weeks	0.9825 (0.9317, 0.9956)	0.9901 (0.9318, 0.9986)
8 Weeks	0.9825 (0.9317, 0.9956)	0.9901 (0.9318, 0.9986)
12 Weeks	0.9382 (0.8747, 0.9701)	0.9801 (0.9228, 0.9950)
16 Weeks	0.9382 (0.8747, 0.9701)	0.9801 (0.9228, 0.9950)
24 Weeks	0.9116 (0.8420, 0.9515)	0.9701 (0.9102, 0.9903)
36 Weeks	0.8585 (0.7794, 0.9108)	0.9495 (0.8828, 0.9787)
52 Weeks	0.8314 (0.7485, 0.8890)	0.9495 (0.8828, 0.9787)
Hazard Ratio (95% CI)*	-	0.2867 (0.1065, 0.7721)
Two-sided P-value, superiority*	-	0.0134

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

ppFEV$_1$ at Baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	7 (8.05)	5 (5.43)
Subjects Censored	80 (91.95)	87 (94.57)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	0.9884 (0.9203, 0.9984)	0.9891 (0.9253, 0.9985)
12 Weeks	0.9884 (0.9203, 0.9984)	0.9783 (0.9159, 0.9945)
16 Weeks	0.9646 (0.8941, 0.9884)	0.9783 (0.9159, 0.9945)
24 Weeks	0.9646 (0.8941, 0.9884)	0.9673 (0.9020, 0.9893)
36 Weeks	0.9168 (0.8333, 0.9594)	0.9562 (0.8874, 0.9833)
52 Weeks	0.9168 (0.8333, 0.9594)	0.9450 (0.8730, 0.9767)
Hazard Ratio (95% CI)*	-	0.6112 (0.1913, 1.9522)
Two-sided P-value, superiority*	-	0.4060

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	2 (6.45)	1 (3.85)
Subjects Censored	29 (93.55)	25 (96.15)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	1.0000 (-, -)
12 Weeks	1.0000 (-, -)	1.0000 (-, -)
16 Weeks	1.0000 (-, -)	1.0000 (-, -)
24 Weeks	1.0000 (-, -)	1.0000 (-, -)
36 Weeks	0.9643 (0.7724, 0.9949)	1.0000 (-, -)
52 Weeks	0.9286 (0.7435, 0.9816)	0.9600 (0.7484, 0.9943)
Hazard Ratio (95% CI)*	-	0.3035 (0.0187, 4.9211)
Two-sided P-value, superiority*	-	0.4015

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	24 (14.04)	9 (5.29)
Subjects Censored	147 (85.96)	161 (94.71)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9883 (0.9540, 0.9971)	0.9941 (0.9590, 0.9992)
4 Weeks	0.9883 (0.9540, 0.9971)	0.9941 (0.9590, 0.9992)
8 Weeks	0.9824 (0.9465, 0.9943)	0.9882 (0.9538, 0.9970)
12 Weeks	0.9529 (0.9080, 0.9762)	0.9764 (0.9383, 0.9911)
16 Weeks	0.9411 (0.8932, 0.9678)	0.9764 (0.9383, 0.9911)
24 Weeks	0.9233 (0.8716, 0.9547)	0.9645 (0.9228, 0.9839)
36 Weeks	0.8700 (0.8092, 0.9124)	0.9463 (0.8994, 0.9717)
52 Weeks	0.8578 (0.7953, 0.9023)	0.9463 (0.8994, 0.9717)
Hazard Ratio (95% CI)*	-	0.3696 (0.1716, 0.7961)
Two-sided P-value, superiority*	-	0.0110

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	5 (26.32)	0
Subjects Censored	14 (73.68)	17 (100.00)
Event-free time (weeks)		
75 percent subjects	45.5714	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
4 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
8 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
12 Weeks	0.8421 (0.5865, 0.9462)	1.0000 (-, -)
16 Weeks	0.8421 (0.5865, 0.9462)	1.0000 (-, -)
24 Weeks	0.7895 (0.5319, 0.9153)	1.0000 (-, -)
36 Weeks	0.7895 (0.5319, 0.9153)	1.0000 (-, -)
52 Weeks	0.7331 (0.4723, 0.8794)	1.0000 (-, -)
Hazard Ratio (95% CI)*	-	N/C
Two-sided P-value, superiority*	-	0.9958

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	21 (11.54)	10 (5.65)
Subjects Censored	161 (88.46)	167 (94.35)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9945 (0.9616, 0.9992)	0.9944 (0.9606, 0.9992)
4 Weeks	0.9945 (0.9616, 0.9992)	0.9944 (0.9606, 0.9992)
8 Weeks	0.9889 (0.9565, 0.9972)	0.9887 (0.9556, 0.9972)
12 Weeks	0.9722 (0.9345, 0.9883)	0.9773 (0.9407, 0.9914)
16 Weeks	0.9610 (0.9199, 0.9812)	0.9773 (0.9407, 0.9914)
24 Weeks	0.9497 (0.9056, 0.9735)	0.9659 (0.9256, 0.9845)
36 Weeks	0.8934 (0.8380, 0.9307)	0.9484 (0.9032, 0.9728)
52 Weeks	0.8819 (0.8247, 0.9214)	0.9426 (0.8959, 0.9687)
Hazard Ratio (95% CI)*	-	0.4894 (0.2303, 1.0397)
Two-sided P-value, superiority*	-	0.0631

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	12 (10.08)	4 (3.45)
Subjects Censored	107 (89.92)	112 (96.55)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9914 (0.9404, 0.9988)
4 Weeks	1.0000 (-, -)	0.9914 (0.9404, 0.9988)
8 Weeks	1.0000 (-, -)	0.9914 (0.9404, 0.9988)
12 Weeks	0.9742 (0.9222, 0.9916)	0.9828 (0.9328, 0.9957)
16 Weeks	0.9656 (0.9109, 0.9869)	0.9828 (0.9328, 0.9957)
24 Weeks	0.9483 (0.8886, 0.9765)	0.9741 (0.9217, 0.9916)
36 Weeks	0.9137 (0.8455, 0.9526)	0.9652 (0.9099, 0.9868)
52 Weeks	0.8960 (0.8242, 0.9396)	0.9652 (0.9099, 0.9868)
Hazard Ratio (95% CI)*	-	0.3120 (0.0999, 0.9745)
Two-sided P-value, superiority*	-	0.0450

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	14 (16.87)	6 (7.50)
Subjects Censored	69 (83.13)	74 (92.50)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9759 (0.9071, 0.9939)	1.0000 (-, -)
4 Weeks	0.9759 (0.9071, 0.9939)	1.0000 (-, -)
8 Weeks	0.9639 (0.8921, 0.9882)	0.9875 (0.9146, 0.9982)
12 Weeks	0.9396 (0.8610, 0.9744)	0.9748 (0.9031, 0.9936)
16 Weeks	0.9274 (0.8455, 0.9667)	0.9748 (0.9031, 0.9936)
24 Weeks	0.9152 (0.8303, 0.9586)	0.9620 (0.8868, 0.9876)
36 Weeks	0.8418 (0.7432, 0.9049)	0.9358 (0.8526, 0.9728)
52 Weeks	0.8291 (0.7284, 0.8950)	0.9225 (0.8354, 0.9644)
Hazard Ratio (95% CI)*	-	0.4474 (0.1710, 1.1709)
Two-sided P-value, superiority*	-	0.1013

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	13 (14.29)	5 (5.75)
Subjects Censored	78 (85.71)	82 (94.25)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9890 (0.9246, 0.9984)	0.9885 (0.9212, 0.9984)
4 Weeks	0.9890 (0.9246, 0.9984)	0.9885 (0.9212, 0.9984)
8 Weeks	0.9779 (0.9145, 0.9944)	0.9885 (0.9212, 0.9984)
12 Weeks	0.9668 (0.9006, 0.9892)	0.9770 (0.9112, 0.9942)
16 Weeks	0.9557 (0.8862, 0.9831)	0.9770 (0.9112, 0.9942)
24 Weeks	0.9446 (0.8719, 0.9765)	0.9654 (0.8965, 0.9887)
36 Weeks	0.8890 (0.8035, 0.9387)	0.9533 (0.8803, 0.9822)
52 Weeks	0.8554 (0.7640, 0.9133)	0.9409 (0.8638, 0.9750)
Hazard Ratio (95% CI)*	-	0.4029 (0.1435, 1.1307)
Two-sided P-value, superiority*	-	0.0842

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	13 (11.71)	5 (4.59)
Subjects Censored	98 (88.29)	104 (95.41)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9910 (0.9378, 0.9987)	1.0000 (-, -)
4 Weeks	0.9910 (0.9378, 0.9987)	1.0000 (-, -)
8 Weeks	0.9910 (0.9378, 0.9987)	0.9908 (0.9367, 0.9987)
12 Weeks	0.9541 (0.8932, 0.9806)	0.9816 (0.9283, 0.9954)
16 Weeks	0.9448 (0.8813, 0.9748)	0.9816 (0.9283, 0.9954)
24 Weeks	0.9263 (0.8581, 0.9625)	0.9722 (0.9163, 0.9910)
36 Weeks	0.8800 (0.8023, 0.9285)	0.9535 (0.8919, 0.9804)
52 Weeks	0.8800 (0.8023, 0.9285)	0.9535 (0.8919, 0.9804)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Hazard Ratio (95% CI)*	-	0.3767 (0.1342, 1.0574)
Two-sided P-value, superiority*	-	0.0637

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.9.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

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

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.0800
Age at screening (<18 years vs. ≥18 years) [2]	0.9395
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.1486
Sex (Male vs. Female) [1]	0.5110
Region (North America vs. Rest of the World) [1]	0.5904

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	111	99
Mean (SD)	81.13 (15.67)	83.67 (15.37)
Week 8 (MMRM)		
n	113	98
LS mean (SE)	78.37 (1.74)	84.07 (1.87)
95% CI of LS mean	(74.95, 81.79)	(80.39, 87.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.70 (0.66, 10.73)
Absolute Change at Week 8 (MMRM)		
n	110	96
LS mean (SE)	-2.90 (1.63)	0.45 (1.75)
95% CI of LS mean	(-6.11, 0.32)	(-3.00, 3.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.35 (-1.37, 8.06)
Week 16 (MMRM)		
n	113	98
LS mean (SE)	76.93 (1.74)	84.89 (1.87)
95% CI of LS mean	(73.50, 80.36)	(81.20, 88.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.96 (2.91, 13.00)

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	110	96
LS mean (SE)	-4.05 (1.61)	1.87 (1.72)
95% CI of LS mean	(-7.21, -0.88)	(-1.52, 5.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.92 (1.27, 10.57)
Week 24 (MMRM)		
n	113	97
LS mean (SE)	78.48 (1.78)	82.98 (1.91)
95% CI of LS mean	(74.98, 81.98)	(79.20, 86.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.50 (-0.65, 9.66)
Absolute Change at Week 24 (MMRM)		
n	110	95
LS mean (SE)	-2.77 (1.68)	-0.62 (1.81)
95% CI of LS mean	(-6.09, 0.54)	(-4.19, 2.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.15 (-2.73, 7.03)

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

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Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	112	94
Mean (SD)	78.55 (17.83)	85.48 (14.54)
Absolute Change at Week 52		
n	109	92
Mean (SD)	-3.54 (15.79)	2.32 (14.49)
Week 52 (MMRM)		
n	112	93
LS mean (SE)	78.10 (1.55)	85.55 (1.68)
95% CI of LS mean	(75.05, 81.14)	(82.23, 88.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.45 (2.94, 11.96)
Absolute Change at Week 52 (MMRM)		
n	109	91
LS mean (SE)	-3.40 (1.48)	1.81 (1.60)
95% CI of LS mean	(-6.32, -0.49)	(-1.35, 4.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.22 (0.91, 9.53)

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	110	96
LS mean (SE)	-3.41 (1.27)	1.02 (1.37)
95% CI of LS mean	(-5.92, -0.90)	(-1.68, 3.72)
P-value within Treatment	0.0081	0.4560
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.43 (0.73, 8.13)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0191
Hedges' G (SE)		0.33 (0.14)
Hedges' 95% CI		(0.05, 0.61)
Hedges' P-value		0.0195

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	85	91
Mean (SD)	85.16 (15.53)	88.13 (13.78)
Week 8 (MMRM)		
n	83	90
LS mean (SE)	84.14 (1.64)	86.14 (1.57)
95% CI of LS mean	(80.90, 87.37)	(83.03, 89.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.00 (-2.48, 6.49)
Absolute Change at Week 8 (MMRM)		
n	82	90
LS mean (SE)	-1.20 (1.82)	-2.09 (1.74)
95% CI of LS mean	(-4.80, 2.39)	(-5.53, 1.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.89 (-5.87, 4.09)
Week 16 (MMRM)		
n	83	91
LS mean (SE)	85.40 (1.69)	87.80 (1.62)
95% CI of LS mean	(82.06, 88.74)	(84.60, 91.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.40 (-2.23, 7.02)

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

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Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	82	90
LS mean (SE)	0.28 (1.80)	-0.35 (1.72)
95% CI of LS mean	(-3.27, 3.83)	(-3.74, 3.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.63 (-5.54, 4.29)
Week 24 (MMRM)		
n	83	90
LS mean (SE)	85.94 (1.65)	89.40 (1.58)
95% CI of LS mean	(82.68, 89.19)	(86.28, 92.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.46 (-1.05, 7.98)
Absolute Change at Week 24 (MMRM)		
n	82	89
LS mean (SE)	0.79 (1.84)	1.35 (1.77)
95% CI of LS mean	(-2.85, 4.43)	(-2.14, 4.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.56 (-4.49, 5.61)

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

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Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	79	87
Mean (SD)	86.36 (13.77)	88.83 (12.05)
Absolute Change at Week 52		
n	78	86
Mean (SD)	1.99 (12.23)	0.61 (15.19)
Week 52 (MMRM)		
n	78	87
LS mean (SE)	86.37 (1.44)	89.05 (1.37)
95% CI of LS mean	(83.54, 89.21)	(86.35, 91.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.68 (-1.24, 6.60)
Absolute Change at Week 52 (MMRM)		
n	77	86
LS mean (SE)	1.39 (1.58)	0.87 (1.50)
95% CI of LS mean	(-1.73, 4.50)	(-2.10, 3.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.52 (-4.83, 3.78)

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	82	90
LS mean (SE)	0.82 (1.45)	0.62 (1.39)
95% CI of LS mean	(-2.05, 3.68)	(-2.12, 3.37)
P-value within Treatment	0.5730	0.6546
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.20 (-4.17, 3.77)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9222
Hedges' G (SE)		-0.01 (0.15)
Hedges' 95% CI		(-0.31, 0.29)
Hedges' P-value		0.9221

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

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Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	29	25
Mean (SD)	88.51 (13.36)	89.89 (15.69)
Week 8 (MMRM)		
n	29	24
LS mean (SE)	89.13 (2.08)	89.98 (2.28)
95% CI of LS mean	(84.96, 93.30)	(85.40, 94.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.85 (-5.38, 7.07)
Absolute Change at Week 8 (MMRM)		
n	28	24
LS mean (SE)	-0.29 (2.66)	1.52 (2.90)
95% CI of LS mean	(-5.63, 5.05)	(-4.31, 7.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.81 (-6.14, 9.75)
Week 16 (MMRM)		
n	29	24
LS mean (SE)	89.38 (2.25)	89.01 (2.48)
95% CI of LS mean	(84.86, 93.90)	(84.04, 93.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.37 (-7.13, 6.39)

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	28	23
LS mean (SE)	-0.01 (2.75)	0.84 (3.03)
95% CI of LS mean	(-5.53, 5.52)	(-5.26, 6.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.84 (-7.43, 9.12)
Week 24 (MMRM)		
n	29	24
LS mean (SE)	90.27 (2.90)	88.35 (3.19)
95% CI of LS mean	(84.44, 96.11)	(81.94, 94.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.92 (-10.61, 6.77)
Absolute Change at Week 24 (MMRM)		
n	28	23
LS mean (SE)	0.89 (3.65)	0.44 (4.02)
95% CI of LS mean	(-6.44, 8.22)	(-7.63, 8.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.45 (-11.38, 10.49)

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

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Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	27	25
Mean (SD)	86.52 (15.23)	90.67 (13.75)
Absolute Change at Week 52		
n	26	24
Mean (SD)	-3.53 (14.67)	1.50 (19.91)
Week 52 (MMRM)		
n	27	24
LS mean (SE)	86.09 (2.72)	89.99 (2.92)
95% CI of LS mean	(80.63, 91.56)	(84.11, 95.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.89 (-4.16, 11.95)
Absolute Change at Week 52 (MMRM)		
n	26	23
LS mean (SE)	-3.59 (3.41)	1.78 (3.70)
95% CI of LS mean	(-10.44, 3.26)	(-5.65, 9.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.37 (-4.77, 15.51)

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	28	23
LS mean (SE)	-0.90 (2.81)	1.02 (3.08)
95% CI of LS mean	(-6.54, 4.73)	(-5.18, 7.22)
P-value within Treatment	0.7489	0.7423
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.92 (-6.49, 10.34)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6483
Hedges' G (SE)		0.13 (0.28)
Hedges' 95% CI		(-0.43, 0.69)
Hedges' P-value		0.6472

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

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Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	81.98 (15.88)	85.20 (14.55)
Week 8 (MMRM)		
n	167	164
LS mean (SE)	79.65 (1.37)	84.05 (1.38)
95% CI of LS mean	(76.96, 82.35)	(81.34, 86.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.40 (0.57, 8.23)
Absolute Change at Week 8 (MMRM)		
n	164	162
LS mean (SE)	-2.49 (1.35)	-1.13 (1.36)
95% CI of LS mean	(-5.14, 0.16)	(-3.80, 1.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.36 (-2.40, 5.12)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	79.23 (1.38)	85.59 (1.39)
95% CI of LS mean	(76.52, 81.94)	(82.87, 88.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.36 (2.52, 10.20)

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	-2.58 (1.32)	0.79 (1.32)
95% CI of LS mean	(-5.17, 0.01)	(-1.81, 3.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.37 (-0.30, 7.04)
Week 24 (MMRM)		
n	167	163
LS mean (SE)	80.41 (1.34)	85.45 (1.35)
95% CI of LS mean	(77.78, 83.05)	(82.79, 88.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.04 (1.29, 8.79)
Absolute Change at Week 24 (MMRM)		
n	164	161
LS mean (SE)	-1.63 (1.32)	0.29 (1.33)
95% CI of LS mean	(-4.22, 0.97)	(-2.32, 2.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.92 (-1.76, 5.60)

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

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Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	81.08 (16.81)	86.56 (13.32)
Absolute Change at Week 52		
n	162	156
Mean (SD)	-0.86 (14.59)	1.51 (13.85)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	81.06 (1.17)	86.58 (1.19)
95% CI of LS mean	(78.76, 83.36)	(84.25, 88.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.52 (2.24, 8.80)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	-1.01 (1.13)	1.30 (1.15)
95% CI of LS mean	(-3.24, 1.21)	(-0.96, 3.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.31 (-0.86, 5.48)

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	-1.74 (1.02)	0.79 (1.02)
95% CI of LS mean	(-3.74, 0.26)	(-1.22, 2.80)
P-value within Treatment	0.0877	0.4382
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.53 (-0.30, 5.37)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0798
Hedges' G (SE)		0.19 (0.11)
Hedges' 95% CI		(-0.02, 0.41)
Hedges' P-value		0.0804

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

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Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	82.16 (14.65)	78.47 (22.58)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	81.91 (3.76)	86.41 (4.11)
95% CI of LS mean	(74.24, 89.58)	(78.04, 94.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.50 (-7.01, 16.01)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	-0.32 (4.64)	8.02 (5.07)
95% CI of LS mean	(-9.77, 9.13)	(-2.30, 18.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.34 (-5.82, 22.50)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	79.86 (3.84)	85.02 (4.19)
95% CI of LS mean	(72.04, 87.69)	(76.48, 93.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.16 (-6.58, 16.90)

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-2.37 (4.47)	6.63 (4.88)
95% CI of LS mean	(-11.47, 6.73)	(-3.31, 16.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.00 (-4.66, 22.66)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	79.57 (3.87)	87.45 (4.22)
95% CI of LS mean	(71.66, 87.48)	(78.81, 96.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.88 (-3.98, 19.75)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	-2.66 (4.86)	9.06 (5.31)
95% CI of LS mean	(-12.59, 7.27)	(-1.78, 19.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.72 (-3.14, 26.59)

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

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Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	81.17 (18.68)	82.54 (17.55)
Absolute Change at Week 52		
n	18	13
Mean (SD)	-3.09 (14.03)	4.27 (17.74)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	79.91 (4.17)	81.53 (4.80)
95% CI of LS mean	(71.39, 88.43)	(71.75, 91.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.62 (-11.47, 14.71)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	-2.83 (3.86)	3.68 (4.42)
95% CI of LS mean	(-10.76, 5.10)	(-5.37, 12.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.51 (-5.69, 18.71)

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	-2.62 (3.66)	6.46 (4.02)
95% CI of LS mean	(-10.10, 4.86)	(-1.76, 14.68)
P-value within Treatment	0.4794	0.1191
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.08 (-2.24, 20.40)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1119
Hedges' G (SE)		0.55 (0.34)
Hedges' 95% CI		(-0.13, 1.24)
Hedges' P-value		0.1107

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

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Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	177	174
Mean (SD)	83.11 (15.82)	86.54 (13.71)
Week 8 (MMRM)		
n	177	172
LS mean (SE)	80.87 (1.28)	84.81 (1.30)
95% CI of LS mean	(78.36, 83.38)	(82.26, 87.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.93 (0.36, 7.51)
Absolute Change at Week 8 (MMRM)		
n	173	170
LS mean (SE)	-2.39 (1.25)	-1.59 (1.26)
95% CI of LS mean	(-4.85, 0.07)	(-4.08, 0.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.80 (-2.70, 4.30)
Week 16 (MMRM)		
n	177	173
LS mean (SE)	80.72 (1.30)	86.27 (1.31)
95% CI of LS mean	(78.17, 83.28)	(83.68, 88.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.54 (1.91, 9.17)

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	173	170
LS mean (SE)	-2.20 (1.24)	0.27 (1.25)
95% CI of LS mean	(-4.63, 0.24)	(-2.18, 2.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.47 (-0.99, 5.93)
Week 24 (MMRM)		
n	177	171
LS mean (SE)	82.01 (1.28)	85.80 (1.30)
95% CI of LS mean	(79.49, 84.52)	(83.24, 88.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.79 (0.21, 7.38)
Absolute Change at Week 24 (MMRM)		
n	173	168
LS mean (SE)	-1.12 (1.27)	-0.49 (1.28)
95% CI of LS mean	(-3.61, 1.37)	(-3.01, 2.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-2.92, 4.18)

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

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Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	173	169
Mean (SD)	82.00 (16.51)	87.65 (12.88)
Absolute Change at Week 52		
n	169	166
Mean (SD)	-1.04 (14.72)	1.34 (14.55)
Week 52 (MMRM)		
n	172	167
LS mean (SE)	81.92 (1.10)	87.53 (1.12)
95% CI of LS mean	(79.75, 84.09)	(85.33, 89.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.61 (2.52, 8.71)
Absolute Change at Week 52 (MMRM)		
n	168	164
LS mean (SE)	-1.28 (1.13)	1.09 (1.14)
95% CI of LS mean	(-3.50, 0.95)	(-1.16, 3.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.36 (-0.80, 5.52)

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	173	170
LS mean (SE)	-1.53 (0.98)	0.29 (0.99)
95% CI of LS mean	(-3.46, 0.41)	(-1.66, 2.25)
P-value within Treatment	0.1210	0.7694
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.82 (-0.93, 4.57)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1940
Hedges' G (SE)		0.14 (0.11)
Hedges' 95% CI		(-0.07, 0.35)
Hedges' P-value		0.1944

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	114	115
Mean (SD)	85.26 (16.00)	85.89 (15.26)
Week 8 (MMRM)		
n	115	116
LS mean (SE)	81.58 (1.60)	85.15 (1.60)
95% CI of LS mean	(78.42, 84.73)	(82.00, 88.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.58 (-0.89, 8.05)
Absolute Change at Week 8 (MMRM)		
n	111	115
LS mean (SE)	-3.79 (1.66)	-0.84 (1.63)
95% CI of LS mean	(-7.05, -0.53)	(-4.05, 2.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.95 (-1.64, 7.54)
Week 16 (MMRM)		
n	115	115
LS mean (SE)	81.98 (1.67)	86.29 (1.67)
95% CI of LS mean	(78.69, 85.27)	(82.99, 89.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.31 (-0.36, 8.97)

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	111	114
LS mean (SE)	-2.87 (1.70)	0.30 (1.68)
95% CI of LS mean	(-6.22, 0.49)	(-3.02, 3.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.16 (-1.56, 7.89)
Week 24 (MMRM)		
n	115	114
LS mean (SE)	83.12 (1.54)	87.72 (1.55)
95% CI of LS mean	(80.08, 86.16)	(84.67, 90.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.60 (0.28, 8.92)
Absolute Change at Week 24 (MMRM)		
n	111	113
LS mean (SE)	-2.06 (1.65)	2.06 (1.63)
95% CI of LS mean	(-5.31, 1.19)	(-1.15, 5.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.12 (-0.46, 8.70)

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	113	111
Mean (SD)	84.29 (16.26)	86.56 (13.46)
Absolute Change at Week 52		
n	109	110
Mean (SD)	-1.27 (13.38)	0.93 (14.04)
Week 52 (MMRM)		
n	112	111
LS mean (SE)	83.67 (1.38)	87.00 (1.38)
95% CI of LS mean	(80.95, 86.39)	(84.27, 89.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.33 (-0.54, 7.19)
Absolute Change at Week 52 (MMRM)		
n	108	110
LS mean (SE)	-1.63 (1.31)	1.11 (1.30)
95% CI of LS mean	(-4.21, 0.96)	(-1.45, 3.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.73 (-0.92, 6.39)

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	114
LS mean (SE)	-2.19 (1.31)	1.15 (1.30)
95% CI of LS mean	(-4.77, 0.40)	(-1.40, 3.71)
P-value within Treatment	0.0968	0.3737
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.34 (-0.30, 6.99)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0723
Hedges' G (SE)		0.24 (0.13)
Hedges' 95% CI		(-0.02, 0.50)
Hedges' P-value		0.0723

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	77
Mean (SD)	79.75 (14.73)	85.68 (14.04)
Week 8 (MMRM)		
n	81	72
LS mean (SE)	79.98 (1.86)	84.75 (1.97)
95% CI of LS mean	(76.30, 83.65)	(80.86, 88.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.77 (-0.59, 10.12)
Absolute Change at Week 8 (MMRM)		
n	81	71
LS mean (SE)	-0.21 (1.77)	-0.37 (1.89)
95% CI of LS mean	(-3.71, 3.30)	(-4.11, 3.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.16 (-5.29, 4.97)
Week 16 (MMRM)		
n	81	74
LS mean (SE)	78.57 (1.78)	86.11 (1.86)
95% CI of LS mean	(75.06, 82.09)	(82.43, 89.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.54 (2.44, 12.63)

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	81	72
LS mean (SE)	-1.55 (1.59)	1.92 (1.69)
95% CI of LS mean	(-4.70, 1.59)	(-1.42, 5.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.48 (-1.12, 8.07)
Week 24 (MMRM)		
n	81	73
LS mean (SE)	79.70 (1.97)	83.32 (2.07)
95% CI of LS mean	(75.81, 83.60)	(79.22, 87.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.61 (-2.05, 9.28)
Absolute Change at Week 24 (MMRM)		
n	81	71
LS mean (SE)	-0.42 (1.86)	-2.16 (1.99)
95% CI of LS mean	(-4.11, 3.26)	(-6.09, 1.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.73 (-7.13, 3.66)

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

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Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	79	73
Mean (SD)	78.34 (16.72)	87.98 (13.38)
Absolute Change at Week 52		
n	79	70
Mean (SD)	-1.16 (16.21)	2.42 (15.83)
Week 52 (MMRM)		
n	78	69
LS mean (SE)	78.83 (1.70)	87.57 (1.80)
95% CI of LS mean	(75.48, 82.19)	(84.02, 91.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.74 (3.84, 13.64)
Absolute Change at Week 52 (MMRM)		
n	78	67
LS mean (SE)	-1.35 (1.86)	1.96 (2.00)
95% CI of LS mean	(-5.03, 2.32)	(-1.99, 5.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.31 (-2.08, 8.71)

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

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Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	81	72
LS mean (SE)	-1.11 (1.38)	0.57 (1.47)
95% CI of LS mean	(-3.84, 1.62)	(-2.33, 3.48)
P-value within Treatment	0.4224	0.6967
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.69 (-2.31, 5.68)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4059
Hedges' G (SE)		0.13 (0.16)
Hedges' 95% CI		(-0.18, 0.45)
Hedges' P-value		0.4053

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	84.12 (15.14)	85.82 (13.99)
Week 8 (MMRM)		
n	88	83
LS mean (SE)	81.54 (1.87)	85.47 (1.92)
95% CI of LS mean	(77.85, 85.23)	(81.67, 89.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.93 (-1.37, 9.23)
Absolute Change at Week 8 (MMRM)		
n	86	82
LS mean (SE)	-2.94 (1.79)	-0.65 (1.83)
95% CI of LS mean	(-6.47, 0.59)	(-4.27, 2.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.29 (-2.77, 7.35)
Week 16 (MMRM)		
n	89	85
LS mean (SE)	83.54 (1.47)	88.32 (1.50)
95% CI of LS mean	(80.65, 86.43)	(85.36, 91.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.78 (0.64, 8.93)

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

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

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

Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	87	83
LS mean (SE)	-0.79 (1.50)	2.24 (1.54)
95% CI of LS mean	(-3.75, 2.18)	(-0.79, 5.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.03 (-1.22, 7.28)
Week 24 (MMRM)		
n	89	83
LS mean (SE)	82.51 (1.92)	83.92 (1.98)
95% CI of LS mean	(78.71, 86.31)	(80.00, 87.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.41 (-4.05, 6.87)
Absolute Change at Week 24 (MMRM)		
n	87	81
LS mean (SE)	-1.90 (1.90)	-1.77 (1.96)
95% CI of LS mean	(-5.65, 1.84)	(-5.64, 2.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-5.25, 5.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	88	78
Mean (SD)	80.81 (16.61)	87.11 (13.20)
Absolute Change at Week 52		
n	86	76
Mean (SD)	-3.46 (13.30)	1.61 (13.27)
Week 52 (MMRM)		
n	87	77
LS mean (SE)	80.97 (1.58)	87.19 (1.65)
95% CI of LS mean	(77.86, 84.09)	(83.93, 90.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.22 (1.70, 10.73)
Absolute Change at Week 52 (MMRM)		
n	85	75
LS mean (SE)	-3.42 (1.44)	1.31 (1.51)
95% CI of LS mean	(-6.26, -0.57)	(-1.67, 4.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.73 (0.60, 8.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	87	83
LS mean (SE)	-2.04 (1.32)	0.59 (1.36)
95% CI of LS mean	(-4.64, 0.57)	(-2.09, 3.28)
P-value within Treatment	0.1255	0.6636
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.63 (-1.12, 6.38)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1683
Hedges' G (SE)		0.21 (0.15)
Hedges' 95% CI		(-0.09, 0.51)
Hedges' P-value		0.1689

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	109	107
Mean (SD)	81.98 (16.11)	85.80 (15.39)
Week 8 (MMRM)		
n	108	105
LS mean (SE)	80.56 (1.58)	84.56 (1.61)
95% CI of LS mean	(77.44, 83.69)	(81.39, 87.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.00 (-0.45, 8.45)
Absolute Change at Week 8 (MMRM)		
n	106	104
LS mean (SE)	-1.46 (1.64)	-0.94 (1.66)
95% CI of LS mean	(-4.70, 1.78)	(-4.22, 2.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.52 (-4.09, 5.13)
Week 16 (MMRM)		
n	107	104
LS mean (SE)	78.19 (1.87)	84.42 (1.90)
95% CI of LS mean	(74.50, 81.89)	(80.67, 88.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.23 (0.96, 11.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	105	103
LS mean (SE)	-3.31 (1.78)	-0.42 (1.80)
95% CI of LS mean	(-6.83, 0.20)	(-3.98, 3.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.89 (-2.11, 7.89)
Week 24 (MMRM)		
n	107	104
LS mean (SE)	81.12 (1.57)	87.56 (1.59)
95% CI of LS mean	(78.03, 84.21)	(84.42, 90.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.44 (2.03, 10.85)
Absolute Change at Week 24 (MMRM)		
n	105	103
LS mean (SE)	-0.66 (1.62)	1.90 (1.64)
95% CI of LS mean	(-3.85, 2.53)	(-1.32, 5.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.56 (-1.98, 7.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	104	106
Mean (SD)	82.72 (16.75)	87.13 (13.62)
Absolute Change at Week 52		
n	102	104
Mean (SD)	0.65 (15.42)	1.44 (15.78)
Week 52 (MMRM)		
n	103	103
LS mean (SE)	82.41 (1.47)	87.10 (1.48)
95% CI of LS mean	(79.52, 85.31)	(84.19, 90.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.69 (0.58, 8.80)
Absolute Change at Week 52 (MMRM)		
n	101	102
LS mean (SE)	0.38 (1.55)	1.39 (1.56)
95% CI of LS mean	(-2.68, 3.44)	(-1.68, 4.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.01 (-3.33, 5.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	105	103
LS mean (SE)	-1.20 (1.35)	0.96 (1.36)
95% CI of LS mean	(-3.85, 1.46)	(-1.73, 3.64)
P-value within Treatment	0.3756	0.4823
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.15 (-1.62, 5.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2620
Hedges' G (SE)		0.16 (0.14)
Hedges' 95% CI		(-0.12, 0.43)
Hedges' P-value		0.2627

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.2.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by SubgroupsFull Analysis Set

Version: Parents/Caregivers Version

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by SubgroupsFull Analysis Set

Version: Parents/Caregivers Version

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by SubgroupsFull Analysis Set

Version: Parents/Caregivers Version

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by SubgroupsFull Analysis Set

Version: Parents/Caregivers Version

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by SubgroupsFull Analysis Set

Version: Parents/Caregivers Version

Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by SubgroupsFull Analysis Set

Version: Parents/Caregivers Version

Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by SubgroupsFull Analysis Set

Version: Parents/Caregivers Version

Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by SubgroupsFull Analysis Set

Version: Parents/Caregivers Version

Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.8153
Age at screening (<18 years vs. ≥18 years) [2]	0.5609
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.3364
Sex (Male vs. Female) [1]	0.8542
Region (North America vs. Rest of the World) [1]	0.9273

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.4566
Age at screening (<18 years vs. ≥18 years) [2]	0.7510
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.9061
Sex (Male vs. Female) [1]	0.9124
Region (North America vs. Rest of the World) [1]	0.2363

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.5781
Age at screening (<18 years vs. ≥18 years) [2]	0.8925
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.5484
Sex (Male vs. Female) [1]	0.9382
Region (North America vs. Rest of the World) [1]	0.1820

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1117
Age at screening (<18 years vs. ≥18 years) [2]	0.0116
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.5858
Sex (Male vs. Female) [1]	0.1458
Region (North America vs. Rest of the World) [1]	0.7498

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.6374
Age at screening (<18 years vs. ≥18 years) [2]	0.1049
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.1078
Sex (Male vs. Female) [1]	0.8262
Region (North America vs. Rest of the World) [1]	0.7940

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.0697
Age at screening (<18 years vs. ≥18 years) [2]	0.7122
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.3188
Sex (Male vs. Female) [1]	0.5642
Region (North America vs. Rest of the World) [1]	0.6690

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1536
Age at screening (<18 years vs. ≥18 years) [2]	0.9576
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.2094
Sex (Male vs. Female) [1]	0.0355
Region (North America vs. Rest of the World) [1]	0.8422

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1525
Age at screening (<18 years vs. ≥18 years) [2]	0.4447
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.3774
Sex (Male vs. Female) [1]	0.9760
Region (North America vs. Rest of the World) [1]	0.6044

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.3420
Age at screening (<18 years vs. ≥18 years) [2]	0.0749
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.0457
Sex (Male vs. Female) [1]	0.6674
Region (North America vs. Rest of the World) [1]	0.1078

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.0859
Age at screening (<18 years vs. ≥18 years) [2]	0.8917
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.4562
Sex (Male vs. Female) [1]	0.1126
Region (North America vs. Rest of the World) [1]	0.8615

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1735
Age at screening (<18 years vs. ≥18 years) [2]	0.9697
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.9150
Sex (Male vs. Female) [1]	0.1536
Region (North America vs. Rest of the World) [1]	0.6444

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	111	99
Mean (SD)	75.38 (22.44)	74.07 (24.02)
Week 8 (MMRM)		
n	113	98
LS mean (SE)	76.36 (2.16)	74.52 (2.32)
95% CI of LS mean	(72.10, 80.62)	(69.95, 79.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.84 (-8.11, 4.42)
Absolute Change at Week 8 (MMRM)		
n	110	96
LS mean (SE)	1.07 (1.29)	0.43 (1.39)
95% CI of LS mean	(-1.49, 3.62)	(-2.30, 3.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-4.39, 3.11)
Week 16 (MMRM)		
n	113	98
LS mean (SE)	76.02 (2.09)	77.04 (2.24)
95% CI of LS mean	(71.90, 80.13)	(72.62, 81.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.02 (-5.04, 7.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	110	96
LS mean (SE)	0.22 (1.35)	3.41 (1.44)
95% CI of LS mean	(-2.44, 2.87)	(0.56, 6.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.19 (-0.71, 7.09)
Week 24 (MMRM)		
n	113	98
LS mean (SE)	76.21 (2.22)	76.30 (2.38)
95% CI of LS mean	(71.84, 80.59)	(71.60, 80.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-6.35, 6.52)
Absolute Change at Week 24 (MMRM)		
n	110	96
LS mean (SE)	0.41 (1.51)	2.65 (1.61)
95% CI of LS mean	(-2.56, 3.38)	(-0.53, 5.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.24 (-2.12, 6.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	112	94
Mean (SD)	77.58 (22.02)	77.66 (21.46)
Absolute Change at Week 52		
n	109	92
Mean (SD)	1.94 (14.96)	2.78 (14.79)
Week 52 (MMRM)		
n	112	93
LS mean (SE)	77.46 (2.07)	77.13 (2.24)
95% CI of LS mean	(73.38, 81.54)	(72.72, 81.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-6.36, 5.70)
Absolute Change at Week 52 (MMRM)		
n	109	91
LS mean (SE)	1.88 (1.44)	3.21 (1.57)
95% CI of LS mean	(-0.97, 4.72)	(0.12, 6.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.34 (-2.88, 5.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	110	96
LS mean (SE)	0.83 (1.18)	3.09 (1.27)
95% CI of LS mean	(-1.50, 3.17)	(0.59, 5.59)
P-value within Treatment	0.4809	0.0158
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.26 (-1.18, 5.69)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1966
Hedges' G (SE)		0.18 (0.14)
Hedges' 95% CI		(-0.09, 0.46)
Hedges' P-value		0.1959

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	85	91
Mean (SD)	78.95 (19.92)	81.56 (21.42)
Week 8 (MMRM)		
n	84	90
LS mean (SE)	81.26 (2.14)	83.70 (2.06)
95% CI of LS mean	(77.04, 85.48)	(79.64, 87.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.44 (-3.42, 8.30)
Absolute Change at Week 8 (MMRM)		
n	83	90
LS mean (SE)	2.14 (1.35)	2.41 (1.30)
95% CI of LS mean	(-0.53, 4.81)	(-0.15, 4.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.27 (-3.44, 3.97)
Week 16 (MMRM)		
n	83	91
LS mean (SE)	80.57 (2.19)	83.27 (2.10)
95% CI of LS mean	(76.25, 84.89)	(79.12, 87.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.70 (-3.30, 8.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	82	90
LS mean (SE)	1.77 (1.51)	1.96 (1.44)
95% CI of LS mean	(-1.20, 4.74)	(-0.88, 4.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.19 (-3.93, 4.30)
Week 24 (MMRM)		
n	83	90
LS mean (SE)	77.22 (2.27)	82.49 (2.18)
95% CI of LS mean	(72.75, 81.69)	(78.19, 86.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.26 (-0.94, 11.47)
Absolute Change at Week 24 (MMRM)		
n	82	89
LS mean (SE)	-1.61 (1.69)	1.37 (1.62)
95% CI of LS mean	(-4.95, 1.72)	(-1.83, 4.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.98 (-1.64, 7.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	80	87
Mean (SD)	81.11 (18.06)	82.76 (19.60)
Absolute Change at Week 52		
n	79	86
Mean (SD)	1.41 (14.05)	1.55 (13.65)
Week 52 (MMRM)		
n	79	87
LS mean (SE)	80.51 (2.08)	82.65 (1.99)
95% CI of LS mean	(76.40, 84.62)	(78.72, 86.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.14 (-3.55, 7.83)
Absolute Change at Week 52 (MMRM)		
n	78	86
LS mean (SE)	1.25 (1.56)	1.50 (1.48)
95% CI of LS mean	(-1.82, 4.32)	(-1.44, 4.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.24 (-4.00, 4.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	82	90
LS mean (SE)	0.47 (1.27)	1.61 (1.22)
95% CI of LS mean	(-2.05, 2.98)	(-0.80, 4.02)
P-value within Treatment	0.7129	0.1892
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.14 (-2.35, 4.62)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5197
Hedges' G (SE)		0.10 (0.15)
Hedges' 95% CI		(-0.20, 0.40)
Hedges' P-value		0.5196

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	29	25
Mean (SD)	75.86 (24.14)	79.11 (27.84)
Week 8 (MMRM)		
n	29	24
LS mean (SE)	82.38 (4.23)	79.25 (4.64)
95% CI of LS mean	(73.89, 90.87)	(69.93, 88.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.13 (-15.81, 9.54)
Absolute Change at Week 8 (MMRM)		
n	28	24
LS mean (SE)	5.89 (2.66)	1.68 (2.89)
95% CI of LS mean	(0.54, 11.24)	(-4.14, 7.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.21 (-12.15, 3.72)
Week 16 (MMRM)		
n	29	24
LS mean (SE)	78.82 (3.90)	82.29 (4.29)
95% CI of LS mean	(70.98, 86.65)	(73.68, 90.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.47 (-8.25, 15.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	28	23
LS mean (SE)	2.41 (2.81)	4.79 (3.10)
95% CI of LS mean	(-3.25, 8.06)	(-1.45, 11.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-6.07, 10.83)
Week 24 (MMRM)		
n	29	24
LS mean (SE)	78.82 (4.41)	77.65 (4.85)
95% CI of LS mean	(69.97, 87.68)	(67.92, 87.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.18 (-14.39, 12.04)
Absolute Change at Week 24 (MMRM)		
n	28	23
LS mean (SE)	2.41 (3.26)	0.45 (3.59)
95% CI of LS mean	(-4.13, 8.96)	(-6.77, 7.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.96 (-11.74, 7.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	28	25
Mean (SD)	80.95 (21.14)	83.56 (21.06)
Absolute Change at Week 52		
n	27	24
Mean (SD)	4.53 (13.87)	6.02 (14.65)
Week 52 (MMRM)		
n	28	24
LS mean (SE)	81.02 (3.78)	82.78 (4.13)
95% CI of LS mean	(73.44, 88.60)	(74.49, 91.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.76 (-9.55, 13.07)
Absolute Change at Week 52 (MMRM)		
n	27	23
LS mean (SE)	4.74 (2.78)	5.91 (3.04)
95% CI of LS mean	(-0.85, 10.34)	(-0.20, 12.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.16 (-7.15, 9.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	28	23
LS mean (SE)	3.19 (2.45)	3.71 (2.71)
95% CI of LS mean	(-1.75, 8.12)	(-1.73, 9.15)
P-value within Treatment	0.2002	0.1763
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.53 (-6.85, 7.91)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8866
Hedges' G (SE)		0.04 (0.28)
Hedges' 95% CI		(-0.52, 0.60)
Hedges' P-value		0.8860

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	76.72 (21.52)	77.64 (22.29)
Week 8 (MMRM)		
n	168	164
LS mean (SE)	77.77 (1.65)	78.89 (1.66)
95% CI of LS mean	(74.53, 81.01)	(75.62, 82.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.12 (-3.49, 5.73)
Absolute Change at Week 8 (MMRM)		
n	165	162
LS mean (SE)	0.91 (1.00)	1.22 (1.01)
95% CI of LS mean	(-1.06, 2.87)	(-0.77, 3.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.31 (-2.49, 3.10)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	77.79 (1.65)	79.72 (1.66)
95% CI of LS mean	(74.54, 81.03)	(76.44, 82.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.93 (-2.68, 6.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	0.74 (1.07)	2.28 (1.08)
95% CI of LS mean	(-1.37, 2.85)	(0.16, 4.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.54 (-1.45, 4.53)
Week 24 (MMRM)		
n	167	164
LS mean (SE)	76.26 (1.70)	79.52 (1.72)
95% CI of LS mean	(72.91, 79.61)	(76.14, 82.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.26 (-1.50, 8.02)
Absolute Change at Week 24 (MMRM)		
n	164	162
LS mean (SE)	-0.82 (1.20)	2.14 (1.20)
95% CI of LS mean	(-3.17, 1.54)	(-0.23, 4.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.95 (-0.39, 6.30)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	78.45 (20.67)	79.73 (20.60)
Absolute Change at Week 52		
n	162	156
Mean (SD)	1.37 (14.69)	1.64 (14.04)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	78.35 (1.61)	79.31 (1.63)
95% CI of LS mean	(75.19, 81.51)	(76.11, 82.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.96 (-3.54, 5.46)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	1.22 (1.14)	1.69 (1.16)
95% CI of LS mean	(-1.03, 3.47)	(-0.59, 3.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.47 (-2.74, 3.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	0.38 (0.93)	2.04 (0.93)
95% CI of LS mean	(-1.44, 2.20)	(0.20, 3.87)
P-value within Treatment	0.6810	0.0298
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.65 (-0.93, 4.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2094
Hedges' G (SE)		0.14 (0.11)
Hedges' 95% CI		(-0.08, 0.36)
Hedges' P-value		0.2097

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	81.29 (15.74)	67.36 (26.75)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	81.12 (4.63)	73.81 (5.07)
95% CI of LS mean	(71.66, 90.58)	(63.46, 84.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.30 (-21.65, 7.05)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	-0.11 (2.68)	6.38 (2.93)
95% CI of LS mean	(-5.60, 5.37)	(0.39, 12.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.50 (-1.80, 14.80)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	82.87 (4.89)	73.12 (5.35)
95% CI of LS mean	(72.89, 92.85)	(62.20, 84.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.75 (-24.85, 5.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	1.64 (3.29)	5.69 (3.60)
95% CI of LS mean	(-5.07, 8.35)	(-1.64, 13.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.05 (-6.03, 14.13)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	79.95 (5.30)	75.20 (5.79)
95% CI of LS mean	(69.12, 90.78)	(63.37, 87.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.75 (-21.06, 11.57)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	-1.28 (3.58)	7.77 (3.91)
95% CI of LS mean	(-8.58, 6.01)	(-0.19, 15.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.06 (-1.87, 19.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	82.10 (21.61)	66.67 (21.35)
Absolute Change at Week 52		
n	18	13
Mean (SD)	0.00 (17.46)	-3.42 (13.13)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	81.08 (5.84)	63.81 (6.56)
95% CI of LS mean	(68.92, 93.24)	(50.22, 77.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-17.26 (-35.75, 1.23)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	-0.09 (3.77)	-3.43 (4.37)
95% CI of LS mean	(-7.86, 7.68)	(-12.40, 5.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.34 (-15.31, 8.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	0.09 (2.91)	3.35 (3.22)
95% CI of LS mean	(-5.88, 6.05)	(-3.24, 9.93)
P-value within Treatment	0.9759	0.3078
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.26 (-5.79, 12.30)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4673
Hedges' G (SE)		0.25 (0.33)
Hedges' 95% CI		(-0.43, 0.93)
Hedges' P-value		0.4600

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	177	174
Mean (SD)	76.21 (22.40)	78.86 (22.59)
Week 8 (MMRM)		
n	178	172
LS mean (SE)	78.19 (1.64)	79.39 (1.66)
95% CI of LS mean	(74.97, 81.41)	(76.13, 82.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.21 (-3.38, 5.80)
Absolute Change at Week 8 (MMRM)		
n	174	170
LS mean (SE)	1.77 (0.99)	0.86 (1.00)
95% CI of LS mean	(-0.18, 3.72)	(-1.11, 2.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.91 (-3.69, 1.86)
Week 16 (MMRM)		
n	177	173
LS mean (SE)	77.44 (1.60)	80.66 (1.62)
95% CI of LS mean	(74.29, 80.59)	(77.47, 83.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.22 (-1.27, 7.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	173	170
LS mean (SE)	0.86 (1.05)	2.37 (1.06)
95% CI of LS mean	(-1.21, 2.92)	(0.29, 4.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.51 (-1.42, 4.45)
Week 24 (MMRM)		
n	177	172
LS mean (SE)	76.31 (1.68)	79.64 (1.70)
95% CI of LS mean	(73.01, 79.61)	(76.29, 82.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.33 (-1.37, 8.03)
Absolute Change at Week 24 (MMRM)		
n	173	169
LS mean (SE)	-0.30 (1.19)	1.45 (1.20)
95% CI of LS mean	(-2.63, 2.03)	(-0.91, 3.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.75 (-1.57, 5.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	174	169
Mean (SD)	78.61 (20.62)	81.39 (20.31)
Absolute Change at Week 52		
n	170	166
Mean (SD)	2.03 (14.34)	2.61 (14.21)
Week 52 (MMRM)		
n	173	167
LS mean (SE)	78.48 (1.53)	81.05 (1.55)
95% CI of LS mean	(75.48, 81.49)	(78.00, 84.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.56 (-1.72, 6.84)
Absolute Change at Week 52 (MMRM)		
n	169	164
LS mean (SE)	1.83 (1.11)	2.72 (1.12)
95% CI of LS mean	(-0.34, 4.01)	(0.52, 4.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.89 (-2.20, 3.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	173	170
LS mean (SE)	0.80 (0.91)	2.18 (0.92)
95% CI of LS mean	(-1.00, 2.59)	(0.37, 3.99)
P-value within Treatment	0.3825	0.0185
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.38 (-1.17, 3.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2867
Hedges' G (SE)		0.12 (0.11)
Hedges' 95% CI		(-0.10, 0.33)
Hedges' P-value		0.2869

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	114	115
Mean (SD)	74.85 (23.19)	75.07 (25.39)
Week 8 (MMRM)		
n	116	116
LS mean (SE)	76.81 (2.15)	76.92 (2.16)
95% CI of LS mean	(72.57, 81.06)	(72.66, 81.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.11 (-5.92, 6.14)
Absolute Change at Week 8 (MMRM)		
n	112	115
LS mean (SE)	1.60 (1.29)	2.11 (1.28)
95% CI of LS mean	(-0.95, 4.14)	(-0.41, 4.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.51 (-3.08, 4.10)
Week 16 (MMRM)		
n	115	115
LS mean (SE)	76.83 (2.14)	77.89 (2.15)
95% CI of LS mean	(72.61, 81.06)	(73.66, 82.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.06 (-4.95, 7.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	111	114
LS mean (SE)	1.37 (1.39)	3.22 (1.38)
95% CI of LS mean	(-1.38, 4.11)	(0.51, 5.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.85 (-2.02, 5.72)
Week 24 (MMRM)		
n	115	115
LS mean (SE)	74.61 (2.26)	76.20 (2.27)
95% CI of LS mean	(70.16, 79.07)	(71.73, 80.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.59 (-4.74, 7.91)
Absolute Change at Week 24 (MMRM)		
n	111	114
LS mean (SE)	-0.94 (1.56)	1.52 (1.54)
95% CI of LS mean	(-4.02, 2.13)	(-1.52, 4.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.46 (-1.87, 6.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	113	111
Mean (SD)	78.56 (20.88)	77.98 (21.81)
Absolute Change at Week 52		
n	109	110
Mean (SD)	3.26 (14.68)	2.22 (14.42)
Week 52 (MMRM)		
n	112	111
LS mean (SE)	78.48 (1.99)	77.58 (2.00)
95% CI of LS mean	(74.56, 82.41)	(73.64, 81.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.90 (-6.48, 4.68)
Absolute Change at Week 52 (MMRM)		
n	108	110
LS mean (SE)	2.94 (1.41)	2.76 (1.40)
95% CI of LS mean	(0.16, 5.72)	(0.01, 5.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-4.10, 3.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	114
LS mean (SE)	1.12 (1.21)	2.50 (1.20)
95% CI of LS mean	(-1.27, 3.51)	(0.13, 4.86)
P-value within Treatment	0.3567	0.0384
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.38 (-2.00, 4.75)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4219
Hedges' G (SE)		0.11 (0.13)
Hedges' 95% CI		(-0.15, 0.37)
Hedges' P-value		0.4207

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	77
Mean (SD)	78.98 (19.79)	81.96 (18.30)
Week 8 (MMRM)		
n	81	72
LS mean (SE)	81.11 (2.12)	81.69 (2.23)
95% CI of LS mean	(76.92, 85.30)	(77.28, 86.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-5.51, 6.67)
Absolute Change at Week 8 (MMRM)		
n	81	71
LS mean (SE)	1.55 (1.34)	0.07 (1.43)
95% CI of LS mean	(-1.09, 4.20)	(-2.74, 2.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.48 (-5.35, 2.39)
Week 16 (MMRM)		
n	81	74
LS mean (SE)	79.86 (2.03)	83.01 (2.13)
95% CI of LS mean	(75.84, 83.87)	(78.81, 87.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.16 (-2.67, 8.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	81	72
LS mean (SE)	0.37 (1.41)	1.76 (1.49)
95% CI of LS mean	(-2.41, 3.15)	(-1.19, 4.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.39 (-2.67, 5.44)
Week 24 (MMRM)		
n	81	73
LS mean (SE)	79.85 (2.08)	83.75 (2.19)
95% CI of LS mean	(75.74, 83.97)	(79.43, 88.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.90 (-2.08, 9.88)
Absolute Change at Week 24 (MMRM)		
n	81	71
LS mean (SE)	0.37 (1.58)	2.77 (1.68)
95% CI of LS mean	(-2.75, 3.49)	(-0.56, 6.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.40 (-2.16, 6.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	80	73
Mean (SD)	79.17 (20.57)	83.71 (18.34)
Absolute Change at Week 52		
n	80	70
Mean (SD)	-0.14 (14.31)	2.22 (13.85)
Week 52 (MMRM)		
n	79	69
LS mean (SE)	79.39 (2.17)	82.88 (2.29)
95% CI of LS mean	(75.11, 83.68)	(78.35, 87.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.48 (-2.77, 9.73)
Absolute Change at Week 52 (MMRM)		
n	79	67
LS mean (SE)	-0.09 (1.60)	1.54 (1.73)
95% CI of LS mean	(-3.26, 3.07)	(-1.88, 4.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.63 (-3.04, 6.30)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	81	72
LS mean (SE)	0.21 (1.20)	2.02 (1.28)
95% CI of LS mean	(-2.17, 2.59)	(-0.52, 4.56)
P-value within Treatment	0.8592	0.1175
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.81 (-1.68, 5.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3072
Hedges' G (SE)		0.17 (0.16)
Hedges' 95% CI		(-0.15, 0.48)
Hedges' P-value		0.3069

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	78.66 (20.02)	79.61 (22.01)
Week 8 (MMRM)		
n	88	83
LS mean (SE)	80.04 (2.17)	80.47 (2.23)
95% CI of LS mean	(75.75, 84.33)	(76.07, 84.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-5.72, 6.58)
Absolute Change at Week 8 (MMRM)		
n	86	82
LS mean (SE)	1.15 (1.44)	0.83 (1.48)
95% CI of LS mean	(-1.70, 4.00)	(-2.09, 3.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-4.40, 3.77)
Week 16 (MMRM)		
n	89	85
LS mean (SE)	78.19 (2.32)	80.23 (2.37)
95% CI of LS mean	(73.61, 82.76)	(75.55, 84.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.04 (-4.51, 8.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	87	83
LS mean (SE)	-0.48 (1.55)	0.78 (1.58)
95% CI of LS mean	(-3.54, 2.57)	(-2.35, 3.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.26 (-3.12, 5.63)
Week 24 (MMRM)		
n	89	84
LS mean (SE)	78.81 (2.28)	81.29 (2.33)
95% CI of LS mean	(74.32, 83.30)	(76.68, 85.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.48 (-3.96, 8.93)
Absolute Change at Week 24 (MMRM)		
n	87	82
LS mean (SE)	0.15 (1.62)	2.09 (1.67)
95% CI of LS mean	(-3.05, 3.36)	(-1.20, 5.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.94 (-2.66, 6.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	88	78
Mean (SD)	80.43 (19.43)	81.48 (20.31)
Absolute Change at Week 52		
n	86	76
Mean (SD)	1.29 (15.94)	0.73 (16.16)
Week 52 (MMRM)		
n	87	77
LS mean (SE)	80.25 (2.16)	80.47 (2.24)
95% CI of LS mean	(75.98, 84.52)	(76.04, 84.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.22 (-5.94, 6.38)
Absolute Change at Week 52 (MMRM)		
n	85	75
LS mean (SE)	1.29 (1.79)	1.03 (1.88)
95% CI of LS mean	(-2.25, 4.84)	(-2.68, 4.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-5.40, 4.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	87	83
LS mean (SE)	0.32 (1.40)	1.30 (1.44)
95% CI of LS mean	(-2.44, 3.08)	(-1.54, 4.14)
P-value within Treatment	0.8183	0.3675
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.98 (-2.99, 4.94)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6268
Hedges' G (SE)		0.07 (0.15)
Hedges' 95% CI		(-0.23, 0.38)
Hedges' P-value		0.6263

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	109	107
Mean (SD)	74.92 (23.20)	76.43 (23.78)
Week 8 (MMRM)		
n	109	105
LS mean (SE)	77.14 (2.16)	77.77 (2.20)
95% CI of LS mean	(72.87, 81.40)	(73.43, 82.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-5.45, 6.72)
Absolute Change at Week 8 (MMRM)		
n	107	104
LS mean (SE)	2.07 (1.23)	1.59 (1.25)
95% CI of LS mean	(-0.36, 4.49)	(-0.87, 4.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.48 (-3.93, 2.98)
Week 16 (MMRM)		
n	107	104
LS mean (SE)	77.79 (2.03)	79.90 (2.06)
95% CI of LS mean	(73.79, 81.79)	(75.83, 83.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.11 (-3.59, 7.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	105	103
LS mean (SE)	2.26 (1.29)	4.03 (1.30)
95% CI of LS mean	(-0.28, 4.79)	(1.47, 6.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.78 (-1.83, 5.38)
Week 24 (MMRM)		
n	107	104
LS mean (SE)	74.88 (2.23)	77.66 (2.26)
95% CI of LS mean	(70.49, 79.27)	(73.19, 82.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.77 (-3.48, 9.03)
Absolute Change at Week 24 (MMRM)		
n	105	103
LS mean (SE)	-0.71 (1.54)	1.77 (1.55)
95% CI of LS mean	(-3.74, 2.32)	(-1.29, 4.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.48 (-1.83, 6.79)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	105	106
Mean (SD)	77.46 (21.71)	79.35 (20.94)
Absolute Change at Week 52		
n	103	104
Mean (SD)	2.27 (13.42)	3.31 (12.47)
Week 52 (MMRM)		
n	104	103
LS mean (SE)	77.53 (2.01)	79.23 (2.04)
95% CI of LS mean	(73.56, 81.49)	(75.21, 83.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.70 (-3.94, 7.35)
Absolute Change at Week 52 (MMRM)		
n	102	102
LS mean (SE)	2.11 (1.26)	3.22 (1.26)
95% CI of LS mean	(-0.37, 4.60)	(0.73, 5.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.11 (-2.41, 4.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	105	103
LS mean (SE)	1.22 (1.08)	3.01 (1.09)
95% CI of LS mean	(-0.90, 3.34)	(0.86, 5.15)
P-value within Treatment	0.2586	0.0062
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.79 (-1.23, 4.80)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2442
Hedges' G (SE)		0.16 (0.14)
Hedges' 95% CI		(-0.11, 0.43)
Hedges' P-value		0.2449

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	111	98
Mean (SD)	83.63 (17.00)	85.94 (16.47)
Week 8 (MMRM)		
n	113	98
LS mean (SE)	83.01 (1.57)	86.36 (1.68)
95% CI of LS mean	(79.92, 86.09)	(83.04, 89.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.35 (-1.19, 7.89)
Absolute Change at Week 8 (MMRM)		
n	110	95
LS mean (SE)	-1.30 (1.43)	1.24 (1.54)
95% CI of LS mean	(-4.13, 1.52)	(-1.80, 4.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.54 (-1.62, 6.71)
Week 16 (MMRM)		
n	113	98
LS mean (SE)	82.51 (1.73)	84.11 (1.86)
95% CI of LS mean	(79.09, 85.92)	(80.44, 87.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.61 (-3.42, 6.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	110	95
LS mean (SE)	-1.81 (1.47)	-1.65 (1.58)
95% CI of LS mean	(-4.70, 1.08)	(-4.76, 1.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-4.09, 4.42)
Week 24 (MMRM)		
n	113	96
LS mean (SE)	84.19 (1.52)	84.90 (1.63)
95% CI of LS mean	(81.20, 87.18)	(81.67, 88.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.71 (-3.70, 5.12)
Absolute Change at Week 24 (MMRM)		
n	110	94
LS mean (SE)	-0.09 (1.42)	-0.41 (1.53)
95% CI of LS mean	(-2.89, 2.70)	(-3.42, 2.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.32 (-4.44, 3.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	112	94
Mean (SD)	84.72 (14.55)	83.45 (15.35)
Absolute Change at Week 52		
n	109	91
Mean (SD)	0.36 (16.22)	-2.44 (10.32)
Week 52 (MMRM)		
n	112	93
LS mean (SE)	84.80 (1.39)	82.97 (1.51)
95% CI of LS mean	(82.06, 87.53)	(80.00, 85.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.83 (-5.88, 2.22)
Absolute Change at Week 52 (MMRM)		
n	109	90
LS mean (SE)	0.46 (1.31)	-2.28 (1.43)
95% CI of LS mean	(-2.11, 3.04)	(-5.09, 0.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.75 (-6.57, 1.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	110	95
LS mean (SE)	-0.48 (1.19)	-1.45 (1.29)
95% CI of LS mean	(-2.84, 1.88)	(-3.99, 1.10)
P-value within Treatment	0.6885	0.2633
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.97 (-4.44, 2.51)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5845
Hedges' G (SE)		-0.08 (0.14)
Hedges' 95% CI		(-0.35, 0.20)
Hedges' P-value		0.5832

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	85	91
Mean (SD)	81.44 (20.02)	83.76 (14.84)
Week 8 (MMRM)		
n	83	90
LS mean (SE)	80.33 (2.09)	85.99 (2.01)
95% CI of LS mean	(76.20, 84.47)	(82.02, 89.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.65 (-0.08, 11.38)
Absolute Change at Week 8 (MMRM)		
n	82	90
LS mean (SE)	-1.00 (1.68)	2.48 (1.61)
95% CI of LS mean	(-4.31, 2.32)	(-0.70, 5.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.47 (-1.12, 8.07)
Week 16 (MMRM)		
n	83	91
LS mean (SE)	80.28 (2.17)	82.87 (2.08)
95% CI of LS mean	(75.98, 84.57)	(78.76, 86.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.59 (-3.35, 8.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	82	90
LS mean (SE)	-1.09 (1.70)	-0.46 (1.62)
95% CI of LS mean	(-4.44, 2.25)	(-3.66, 2.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.64 (-4.00, 5.28)
Week 24 (MMRM)		
n	83	90
LS mean (SE)	79.95 (1.92)	86.72 (1.85)
95% CI of LS mean	(76.15, 83.74)	(83.08, 90.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.78 (1.51, 12.05)
Absolute Change at Week 24 (MMRM)		
n	82	89
LS mean (SE)	-1.24 (1.44)	3.05 (1.38)
95% CI of LS mean	(-4.08, 1.60)	(0.32, 5.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.28 (0.35, 8.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	79	87
Mean (SD)	79.75 (22.35)	81.23 (19.56)
Absolute Change at Week 52		
n	78	86
Mean (SD)	-0.57 (16.88)	-1.94 (14.88)
Week 52 (MMRM)		
n	78	87
LS mean (SE)	80.63 (2.32)	81.51 (2.22)
95% CI of LS mean	(76.04, 85.21)	(77.13, 85.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.89 (-5.46, 7.23)
Absolute Change at Week 52 (MMRM)		
n	77	86
LS mean (SE)	-0.63 (1.78)	-1.84 (1.70)
95% CI of LS mean	(-4.15, 2.90)	(-5.19, 1.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.21 (-6.08, 3.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	82	90
LS mean (SE)	-0.99 (1.35)	0.25 (1.29)
95% CI of LS mean	(-3.64, 1.67)	(-2.29, 2.79)
P-value within Treatment	0.4645	0.8458
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.24 (-2.44, 4.92)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5078
Hedges' G (SE)		0.10 (0.15)
Hedges' 95% CI		(-0.20, 0.40)
Hedges' P-value		0.5077

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	29	25
Mean (SD)	91.95 (14.21)	87.11 (14.59)
Week 8 (MMRM)		
n	29	24
LS mean (SE)	89.03 (3.78)	83.77 (4.15)
95% CI of LS mean	(81.43, 96.62)	(75.44, 92.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.25 (-16.57, 6.07)
Absolute Change at Week 8 (MMRM)		
n	28	24
LS mean (SE)	-3.43 (2.79)	-0.99 (3.03)
95% CI of LS mean	(-9.03, 2.18)	(-7.08, 5.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.44 (-5.87, 10.74)
Week 16 (MMRM)		
n	29	24
LS mean (SE)	86.35 (4.34)	81.68 (4.76)
95% CI of LS mean	(77.64, 95.07)	(72.12, 91.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.67 (-17.64, 8.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	28	23
LS mean (SE)	-6.22 (3.12)	-2.34 (3.44)
95% CI of LS mean	(-12.49, 0.06)	(-9.27, 4.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.87 (-5.50, 13.24)
Week 24 (MMRM)		
n	29	24
LS mean (SE)	91.91 (2.55)	88.74 (2.81)
95% CI of LS mean	(86.78, 97.05)	(83.09, 94.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.18 (-10.88, 4.52)
Absolute Change at Week 24 (MMRM)		
n	28	23
LS mean (SE)	-0.30 (2.54)	2.97 (2.80)
95% CI of LS mean	(-5.40, 4.80)	(-2.67, 8.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.27 (-4.37, 10.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	27	25
Mean (SD)	90.12 (17.52)	82.22 (20.79)
Absolute Change at Week 52		
n	26	24
Mean (SD)	-2.99 (13.90)	-3.70 (12.11)
Week 52 (MMRM)		
n	27	24
LS mean (SE)	90.34 (3.68)	79.62 (4.00)
95% CI of LS mean	(82.95, 97.73)	(71.59, 87.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-10.72 (-21.67, 0.24)
Absolute Change at Week 52 (MMRM)		
n	26	23
LS mean (SE)	-2.23 (2.52)	-4.61 (2.73)
95% CI of LS mean	(-7.31, 2.85)	(-10.10, 0.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.38 (-9.89, 5.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	28	23
LS mean (SE)	-2.91 (2.15)	-1.33 (2.37)
95% CI of LS mean	(-7.24, 1.41)	(-6.09, 3.44)
P-value within Treatment	0.1820	0.5777
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.59 (-4.89, 8.07)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6244
Hedges' G (SE)		0.14 (0.28)
Hedges' 95% CI		(-0.42, 0.69)
Hedges' P-value		0.6227

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	166
Mean (SD)	81.05 (18.49)	84.74 (15.88)
Week 8 (MMRM)		
n	167	164
LS mean (SE)	80.55 (1.34)	86.54 (1.35)
95% CI of LS mean	(77.92, 83.19)	(83.88, 89.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.99 (2.24, 9.74)
Absolute Change at Week 8 (MMRM)		
n	164	161
LS mean (SE)	-0.78 (1.18)	2.25 (1.19)
95% CI of LS mean	(-3.10, 1.55)	(-0.10, 4.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.03 (-0.28, 6.33)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	80.66 (1.41)	83.78 (1.42)
95% CI of LS mean	(77.89, 83.44)	(80.98, 86.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.12 (-0.82, 7.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	162
LS mean (SE)	-0.67 (1.18)	-0.90 (1.19)
95% CI of LS mean	(-2.99, 1.65)	(-3.24, 1.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-3.53, 3.07)
Week 24 (MMRM)		
n	167	162
LS mean (SE)	80.66 (1.33)	85.44 (1.34)
95% CI of LS mean	(78.05, 83.27)	(82.80, 88.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.78 (1.07, 8.49)
Absolute Change at Week 24 (MMRM)		
n	164	160
LS mean (SE)	-0.60 (1.10)	1.05 (1.11)
95% CI of LS mean	(-2.77, 1.56)	(-1.14, 3.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.65 (-1.43, 4.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	81.41 (18.12)	82.39 (17.20)
Absolute Change at Week 52		
n	162	155
Mean (SD)	0.45 (16.78)	-1.94 (12.73)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	81.63 (1.35)	82.63 (1.37)
95% CI of LS mean	(78.98, 84.29)	(79.93, 85.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.00 (-2.79, 4.78)
Absolute Change at Week 52 (MMRM)		
n	160	153
LS mean (SE)	0.45 (1.18)	-1.74 (1.20)
95% CI of LS mean	(-1.87, 2.76)	(-4.10, 0.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.19 (-5.49, 1.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	162
LS mean (SE)	-0.28 (0.98)	-0.53 (0.99)
95% CI of LS mean	(-2.20, 1.64)	(-2.47, 1.41)
P-value within Treatment	0.7779	0.5895
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-2.99, 2.47)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8534
Hedges' G (SE)		-0.02 (0.11)
Hedges' 95% CI		(-0.24, 0.20)
Hedges' P-value		0.8533

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	81.87 (18.60)	81.94 (19.40)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	82.70 (4.13)	88.60 (4.51)
95% CI of LS mean	(74.29, 91.11)	(79.41, 97.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.90 (-6.74, 18.53)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	0.39 (4.08)	7.17 (4.45)
95% CI of LS mean	(-7.92, 8.70)	(-1.90, 16.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.78 (-5.69, 19.25)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	82.12 (4.65)	83.74 (5.08)
95% CI of LS mean	(72.62, 91.61)	(73.37, 94.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.62 (-12.60, 15.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-0.19 (4.21)	2.31 (4.60)
95% CI of LS mean	(-8.78, 8.40)	(-7.07, 11.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.50 (-10.37, 15.38)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	83.87 (3.76)	88.60 (4.11)
95% CI of LS mean	(76.20, 91.54)	(80.21, 96.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.73 (-6.84, 16.30)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	1.56 (3.23)	7.17 (3.53)
95% CI of LS mean	(-5.02, 8.15)	(-0.03, 14.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.61 (-4.37, 15.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	88.27 (11.09)	78.57 (21.11)
Absolute Change at Week 52		
n	18	13
Mean (SD)	5.56 (19.15)	1.71 (14.23)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	87.72 (3.49)	83.05 (3.93)
95% CI of LS mean	(80.59, 94.84)	(75.04, 91.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.66 (-15.59, 6.26)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	5.27 (3.87)	2.00 (4.35)
95% CI of LS mean	(-2.63, 13.17)	(-6.86, 10.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.26 (-15.31, 8.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	2.21 (3.37)	3.83 (3.70)
95% CI of LS mean	(-4.66, 9.09)	(-3.72, 11.37)
P-value within Treatment	0.5163	0.3088
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.62 (-8.80, 12.03)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7537
Hedges' G (SE)		0.11 (0.33)
Hedges' 95% CI		(-0.57, 0.78)
Hedges' P-value		0.7487

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	177	173
Mean (SD)	82.77 (18.38)	85.16 (15.36)
Week 8 (MMRM)		
n	177	172
LS mean (SE)	81.62 (1.34)	86.12 (1.36)
95% CI of LS mean	(78.98, 84.26)	(83.44, 88.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.50 (0.73, 8.26)
Absolute Change at Week 8 (MMRM)		
n	173	169
LS mean (SE)	-1.46 (1.12)	1.45 (1.14)
95% CI of LS mean	(-3.67, 0.75)	(-0.79, 3.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.91 (-0.24, 6.06)
Week 16 (MMRM)		
n	177	173
LS mean (SE)	81.33 (1.43)	83.65 (1.45)
95% CI of LS mean	(78.52, 84.14)	(80.80, 86.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.32 (-1.68, 6.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	173	169
LS mean (SE)	-1.76 (1.14)	-1.27 (1.15)
95% CI of LS mean	(-3.99, 0.48)	(-3.54, 0.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.48 (-2.70, 3.67)
Week 24 (MMRM)		
n	177	170
LS mean (SE)	82.07 (1.27)	85.68 (1.29)
95% CI of LS mean	(79.57, 84.58)	(83.13, 88.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.60 (0.03, 7.18)
Absolute Change at Week 24 (MMRM)		
n	173	167
LS mean (SE)	-0.92 (1.06)	0.81 (1.08)
95% CI of LS mean	(-3.01, 1.16)	(-1.31, 2.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.73 (-1.24, 4.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	173	169
Mean (SD)	82.02 (18.81)	82.64 (17.43)
Absolute Change at Week 52		
n	169	165
Mean (SD)	-0.69 (16.07)	-2.42 (12.52)
Week 52 (MMRM)		
n	172	167
LS mean (SE)	82.32 (1.36)	82.25 (1.38)
95% CI of LS mean	(79.65, 85.00)	(79.54, 84.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-3.88, 3.74)
Absolute Change at Week 52 (MMRM)		
n	168	163
LS mean (SE)	-0.63 (1.11)	-2.42 (1.13)
95% CI of LS mean	(-2.81, 1.55)	(-4.64, -0.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.79 (-4.90, 1.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	173	169
LS mean (SE)	-1.10 (0.91)	-0.96 (0.93)
95% CI of LS mean	(-2.90, 0.69)	(-2.78, 0.86)
P-value within Treatment	0.2274	0.2989
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-2.42, 2.70)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9136
Hedges' G (SE)		0.01 (0.11)
Hedges' 95% CI		(-0.20, 0.22)
Hedges' P-value		0.9136

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	114	114
Mean (SD)	84.31 (17.10)	86.35 (14.56)
Week 8 (MMRM)		
n	115	116
LS mean (SE)	82.92 (1.55)	88.24 (1.55)
95% CI of LS mean	(79.87, 85.97)	(85.19, 91.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.32 (0.99, 9.65)
Absolute Change at Week 8 (MMRM)		
n	111	114
LS mean (SE)	-1.69 (1.42)	1.70 (1.41)
95% CI of LS mean	(-4.49, 1.12)	(-1.07, 4.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.39 (-0.56, 7.34)
Week 16 (MMRM)		
n	115	115
LS mean (SE)	82.87 (1.60)	85.94 (1.61)
95% CI of LS mean	(79.71, 86.03)	(82.77, 89.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.07 (-1.42, 7.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	111	113
LS mean (SE)	-1.73 (1.29)	-0.87 (1.28)
95% CI of LS mean	(-4.28, 0.81)	(-3.39, 1.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.87 (-2.73, 4.46)
Week 24 (MMRM)		
n	115	114
LS mean (SE)	83.84 (1.45)	86.69 (1.46)
95% CI of LS mean	(80.97, 86.70)	(83.82, 89.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.85 (-1.22, 6.92)
Absolute Change at Week 24 (MMRM)		
n	111	112
LS mean (SE)	-0.63 (1.20)	0.16 (1.19)
95% CI of LS mean	(-2.99, 1.72)	(-2.18, 2.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.79 (-2.54, 4.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	113	111
Mean (SD)	84.07 (15.42)	84.88 (15.12)
Absolute Change at Week 52		
n	109	109
Mean (SD)	-0.51 (14.22)	-1.12 (11.21)
Week 52 (MMRM)		
n	112	111
LS mean (SE)	84.04 (1.42)	85.12 (1.42)
95% CI of LS mean	(81.25, 86.84)	(82.31, 87.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.08 (-2.90, 5.05)
Absolute Change at Week 52 (MMRM)		
n	108	109
LS mean (SE)	-0.36 (1.22)	-1.27 (1.21)
95% CI of LS mean	(-2.76, 2.04)	(-3.66, 1.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.91 (-4.31, 2.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	113
LS mean (SE)	-0.91 (1.05)	-0.66 (1.04)
95% CI of LS mean	(-2.97, 1.16)	(-2.71, 1.39)
P-value within Treatment	0.3864	0.5266
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.25 (-2.67, 3.17)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8664
Hedges' G (SE)		0.02 (0.13)
Hedges' 95% CI		(-0.24, 0.28)
Hedges' P-value		0.8659

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	77
Mean (SD)	80.39 (19.73)	83.12 (17.16)
Week 8 (MMRM)		
n	81	72
LS mean (SE)	79.77 (2.15)	83.54 (2.26)
95% CI of LS mean	(75.52, 84.03)	(79.07, 88.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.77 (-2.42, 9.95)
Absolute Change at Week 8 (MMRM)		
n	81	71
LS mean (SE)	-0.55 (1.68)	2.11 (1.79)
95% CI of LS mean	(-3.87, 2.77)	(-1.42, 5.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.66 (-2.20, 7.52)
Week 16 (MMRM)		
n	81	74
LS mean (SE)	79.07 (2.33)	80.48 (2.44)
95% CI of LS mean	(74.46, 83.69)	(75.66, 85.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.41 (-5.28, 8.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	81	72
LS mean (SE)	-1.24 (1.96)	-1.29 (2.08)
95% CI of LS mean	(-5.12, 2.63)	(-5.40, 2.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-5.71, 5.61)
Week 24 (MMRM)		
n	81	72
LS mean (SE)	79.72 (2.06)	84.98 (2.17)
95% CI of LS mean	(75.64, 83.80)	(80.69, 89.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.26 (-0.67, 11.20)
Absolute Change at Week 24 (MMRM)		
n	81	71
LS mean (SE)	-0.56 (1.79)	3.04 (1.91)
95% CI of LS mean	(-4.09, 2.98)	(-0.72, 6.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.60 (-1.57, 8.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	79	73
Mean (SD)	80.59 (21.61)	78.54 (20.48)
Absolute Change at Week 52		
n	79	70
Mean (SD)	0.63 (19.12)	-3.81 (14.52)
Week 52 (MMRM)		
n	78	69
LS mean (SE)	80.86 (2.32)	78.33 (2.44)
95% CI of LS mean	(76.28, 85.43)	(73.51, 83.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.52 (-9.18, 4.14)
Absolute Change at Week 52 (MMRM)		
n	78	67
LS mean (SE)	0.55 (1.93)	-3.42 (2.07)
95% CI of LS mean	(-3.26, 4.37)	(-7.51, 0.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.97 (-9.57, 1.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	81	72
LS mean (SE)	-0.41 (1.57)	-0.55 (1.67)
95% CI of LS mean	(-3.52, 2.70)	(-3.86, 2.75)
P-value within Treatment	0.7928	0.7410
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-4.69, 4.41)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9516
Hedges' G (SE)		-0.01 (0.16)
Hedges' 95% CI		(-0.33, 0.31)
Hedges' P-value		0.9514

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	82.77 (18.20)	86.27 (14.51)
Week 8 (MMRM)		
n	88	83
LS mean (SE)	78.70 (1.95)	88.23 (2.00)
95% CI of LS mean	(74.84, 82.55)	(84.28, 92.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.53 (4.01, 15.06)
Absolute Change at Week 8 (MMRM)		
n	86	82
LS mean (SE)	-4.25 (1.60)	2.62 (1.63)
95% CI of LS mean	(-7.40, -1.10)	(-0.60, 5.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.87 (2.36, 11.39)
Week 16 (MMRM)		
n	89	85
LS mean (SE)	80.52 (2.11)	85.11 (2.15)
95% CI of LS mean	(76.36, 84.67)	(80.85, 89.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.59 (-1.36, 10.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	87	83
LS mean (SE)	-2.54 (1.56)	-0.49 (1.60)
95% CI of LS mean	(-5.62, 0.55)	(-3.65, 2.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.05 (-2.37, 6.47)
Week 24 (MMRM)		
n	89	83
LS mean (SE)	82.89 (1.84)	87.13 (1.89)
95% CI of LS mean	(79.26, 86.51)	(83.40, 90.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.24 (-0.97, 9.44)
Absolute Change at Week 24 (MMRM)		
n	87	81
LS mean (SE)	0.02 (1.47)	1.43 (1.51)
95% CI of LS mean	(-2.88, 2.92)	(-1.57, 4.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.41 (-2.76, 5.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	88	78
Mean (SD)	81.31 (20.11)	82.76 (17.97)
Absolute Change at Week 52		
n	86	76
Mean (SD)	-1.36 (17.75)	-2.63 (12.15)
Week 52 (MMRM)		
n	87	77
LS mean (SE)	81.46 (2.04)	82.97 (2.12)
95% CI of LS mean	(77.44, 85.48)	(78.79, 87.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.51 (-4.30, 7.32)
Absolute Change at Week 52 (MMRM)		
n	85	75
LS mean (SE)	-1.39 (1.65)	-2.26 (1.73)
95% CI of LS mean	(-4.65, 1.87)	(-5.69, 1.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.87 (-5.60, 3.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	87	83
LS mean (SE)	-1.30 (1.29)	-0.44 (1.33)
95% CI of LS mean	(-3.84, 1.24)	(-3.06, 2.17)
P-value within Treatment	0.3129	0.7393
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.86 (-2.79, 4.51)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6425
Hedges' G (SE)		0.07 (0.15)
Hedges' 95% CI		(-0.23, 0.37)
Hedges' P-value		0.6421

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	109	106
Mean (SD)	82.57 (18.48)	84.07 (16.59)
Week 8 (MMRM)		
n	108	105
LS mean (SE)	84.26 (1.65)	84.77 (1.68)
95% CI of LS mean	(81.01, 87.52)	(81.46, 88.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-4.14, 5.14)
Absolute Change at Week 8 (MMRM)		
n	106	103
LS mean (SE)	1.39 (1.46)	1.14 (1.49)
95% CI of LS mean	(-1.49, 4.28)	(-1.79, 4.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-4.37, 3.86)
Week 16 (MMRM)		
n	107	104
LS mean (SE)	82.17 (1.77)	82.43 (1.80)
95% CI of LS mean	(78.67, 85.67)	(78.87, 85.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.26 (-4.73, 5.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	105	102
LS mean (SE)	-0.63 (1.56)	-1.62 (1.59)
95% CI of LS mean	(-3.70, 2.45)	(-4.75, 1.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.00 (-5.38, 3.39)
Week 24 (MMRM)		
n	107	103
LS mean (SE)	81.75 (1.59)	84.86 (1.62)
95% CI of LS mean	(78.61, 84.89)	(81.66, 88.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.11 (-1.37, 7.59)
Absolute Change at Week 24 (MMRM)		
n	105	102
LS mean (SE)	-1.05 (1.42)	1.01 (1.44)
95% CI of LS mean	(-3.84, 1.75)	(-1.83, 3.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.06 (-1.92, 6.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	104	106
Mean (SD)	83.76 (16.53)	82.08 (17.52)
Absolute Change at Week 52		
n	102	103
Mean (SD)	1.09 (15.20)	-1.83 (13.03)
Week 52 (MMRM)		
n	103	103
LS mean (SE)	84.01 (1.61)	81.79 (1.63)
95% CI of LS mean	(80.83, 87.20)	(78.57, 85.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.23 (-6.75, 2.30)
Absolute Change at Week 52 (MMRM)		
n	101	101
LS mean (SE)	1.25 (1.40)	-2.08 (1.41)
95% CI of LS mean	(-1.51, 4.01)	(-4.86, 0.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.33 (-7.25, 0.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	105	102
LS mean (SE)	-0.14 (1.24)	-0.90 (1.26)
95% CI of LS mean	(-2.59, 2.31)	(-3.38, 1.59)
P-value within Treatment	0.9095	0.4784
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.75 (-4.24, 2.74)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6704
Hedges' G (SE)		-0.06 (0.14)
Hedges' 95% CI		(-0.33, 0.21)
Hedges' P-value		0.6705

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	111	99
Mean (SD)	93.09 (13.49)	90.24 (14.66)
Week 8 (MMRM)		
n	113	98
LS mean (SE)	91.80 (1.44)	90.74 (1.55)
95% CI of LS mean	(88.95, 94.65)	(87.68, 93.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.05 (-5.24, 3.13)
Absolute Change at Week 8 (MMRM)		
n	110	96
LS mean (SE)	-1.72 (1.17)	0.53 (1.26)
95% CI of LS mean	(-4.04, 0.59)	(-1.95, 3.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.26 (-1.14, 5.66)
Week 16 (MMRM)		
n	113	98
LS mean (SE)	91.16 (1.35)	91.17 (1.45)
95% CI of LS mean	(88.50, 93.82)	(88.32, 94.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-3.90, 3.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	110	96
LS mean (SE)	-2.45 (1.19)	1.15 (1.27)
95% CI of LS mean	(-4.79, -0.11)	(-1.36, 3.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.60 (0.17, 7.03)
Week 24 (MMRM)		
n	113	98
LS mean (SE)	93.69 (1.48)	89.26 (1.59)
95% CI of LS mean	(90.77, 96.61)	(86.12, 92.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.44 (-8.73, -0.14)
Absolute Change at Week 24 (MMRM)		
n	110	96
LS mean (SE)	0.18 (1.14)	-1.05 (1.22)
95% CI of LS mean	(-2.07, 2.43)	(-3.46, 1.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.23 (-4.53, 2.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	112	94
Mean (SD)	94.54 (11.93)	92.20 (15.01)
Absolute Change at Week 52		
n	109	92
Mean (SD)	0.92 (10.38)	1.57 (10.10)
Week 52 (MMRM)		
n	112	93
LS mean (SE)	94.36 (1.27)	91.83 (1.37)
95% CI of LS mean	(91.86, 96.85)	(89.12, 94.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.53 (-6.22, 1.16)
Absolute Change at Week 52 (MMRM)		
n	109	91
LS mean (SE)	0.81 (1.00)	1.70 (1.09)
95% CI of LS mean	(-1.16, 2.77)	(-0.44, 3.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.89 (-2.02, 3.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	110	96
LS mean (SE)	-0.49 (0.86)	0.60 (0.92)
95% CI of LS mean	(-2.19, 1.21)	(-1.22, 2.42)
P-value within Treatment	0.5700	0.5174
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.09 (-1.41, 3.59)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3912
Hedges' G (SE)		0.12 (0.14)
Hedges' 95% CI		(-0.15, 0.39)
Hedges' P-value		0.3899

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	85	91
Mean (SD)	92.42 (15.64)	91.82 (18.43)
Week 8 (MMRM)		
n	84	90
LS mean (SE)	93.02 (1.87)	90.49 (1.80)
95% CI of LS mean	(89.32, 96.71)	(86.93, 94.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.53 (-7.66, 2.60)
Absolute Change at Week 8 (MMRM)		
n	83	90
LS mean (SE)	0.00 (1.09)	-0.42 (1.04)
95% CI of LS mean	(-2.14, 2.15)	(-2.48, 1.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.42 (-3.40, 2.55)
Week 16 (MMRM)		
n	83	91
LS mean (SE)	92.58 (1.81)	89.86 (1.74)
95% CI of LS mean	(89.00, 96.15)	(86.43, 93.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.72 (-7.68, 2.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	82	90
LS mean (SE)	-0.49 (1.19)	-1.35 (1.14)
95% CI of LS mean	(-2.84, 1.86)	(-3.60, 0.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.86 (-4.11, 2.39)
Week 24 (MMRM)		
n	83	90
LS mean (SE)	91.92 (1.85)	91.33 (1.78)
95% CI of LS mean	(88.26, 95.57)	(87.82, 94.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.59 (-5.66, 4.48)
Absolute Change at Week 24 (MMRM)		
n	82	89
LS mean (SE)	-1.16 (1.17)	0.36 (1.12)
95% CI of LS mean	(-3.46, 1.15)	(-1.85, 2.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.52 (-1.68, 4.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	80	87
Mean (SD)	92.50 (13.20)	89.91 (21.54)
Absolute Change at Week 52		
n	79	86
Mean (SD)	-0.14 (10.30)	-1.16 (13.95)
Week 52 (MMRM)		
n	79	87
LS mean (SE)	92.10 (1.95)	89.80 (1.87)
95% CI of LS mean	(88.25, 95.95)	(86.11, 93.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.30 (-7.64, 3.04)
Absolute Change at Week 52 (MMRM)		
n	78	86
LS mean (SE)	-0.95 (1.34)	-1.06 (1.28)
95% CI of LS mean	(-3.59, 1.70)	(-3.59, 1.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.12 (-3.78, 3.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	82	90
LS mean (SE)	-0.86 (1.01)	-0.68 (0.96)
95% CI of LS mean	(-2.85, 1.12)	(-2.59, 1.22)
P-value within Treatment	0.3919	0.4781
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-2.57, 2.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8978
Hedges' G (SE)		0.02 (0.15)
Hedges' 95% CI		(-0.28, 0.32)
Hedges' P-value		0.8978

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	29	25
Mean (SD)	90.80 (16.01)	81.78 (29.90)
Week 8 (MMRM)		
n	29	24
LS mean (SE)	88.55 (4.79)	78.67 (5.25)
95% CI of LS mean	(78.94, 98.16)	(68.12, 89.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.88 (-24.23, 4.47)
Absolute Change at Week 8 (MMRM)		
n	28	24
LS mean (SE)	-1.69 (2.63)	-0.77 (2.86)
95% CI of LS mean	(-6.96, 3.59)	(-6.51, 4.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.92 (-6.90, 8.74)
Week 16 (MMRM)		
n	29	24
LS mean (SE)	87.37 (4.28)	81.30 (4.70)
95% CI of LS mean	(78.78, 95.96)	(71.87, 90.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.06 (-18.92, 6.79)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	28	23
LS mean (SE)	-2.72 (2.45)	0.76 (2.70)
95% CI of LS mean	(-7.64, 2.21)	(-4.67, 6.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.47 (-3.89, 10.84)
Week 24 (MMRM)		
n	29	24
LS mean (SE)	90.05 (4.23)	79.45 (4.65)
95% CI of LS mean	(81.55, 98.55)	(70.12, 88.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-10.60 (-23.32, 2.11)
Absolute Change at Week 24 (MMRM)		
n	28	23
LS mean (SE)	0.09 (2.26)	-0.29 (2.50)
95% CI of LS mean	(-4.46, 4.64)	(-5.32, 4.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-7.20, 6.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	28	25
Mean (SD)	90.87 (15.44)	79.11 (33.07)
Absolute Change at Week 52		
n	27	24
Mean (SD)	-0.82 (11.08)	0.46 (20.59)
Week 52 (MMRM)		
n	28	24
LS mean (SE)	88.96 (4.55)	80.39 (4.98)
95% CI of LS mean	(79.83, 98.10)	(70.40, 90.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.57 (-22.19, 5.05)
Absolute Change at Week 52 (MMRM)		
n	27	23
LS mean (SE)	-1.18 (3.16)	1.41 (3.45)
95% CI of LS mean	(-7.52, 5.16)	(-5.52, 8.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.59 (-6.83, 12.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	28	23
LS mean (SE)	-1.27 (2.33)	0.63 (2.56)
95% CI of LS mean	(-5.95, 3.41)	(-4.53, 5.78)
P-value within Treatment	0.5885	0.8083
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.89 (-5.11, 8.90)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5891
Hedges' G (SE)		0.15 (0.28)
Hedges' 95% CI		(-0.41, 0.71)
Hedges' P-value		0.5877

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	93.19 (14.12)	92.48 (12.98)
Week 8 (MMRM)		
n	168	164
LS mean (SE)	92.64 (1.06)	92.74 (1.07)
95% CI of LS mean	(90.55, 94.72)	(90.63, 94.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-2.86, 3.06)
Absolute Change at Week 8 (MMRM)		
n	165	162
LS mean (SE)	-0.83 (0.84)	0.18 (0.85)
95% CI of LS mean	(-2.49, 0.82)	(-1.49, 1.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.01 (-1.34, 3.37)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	92.23 (1.03)	92.31 (1.03)
95% CI of LS mean	(90.21, 94.25)	(90.28, 94.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-2.79, 2.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	-1.40 (0.90)	-0.19 (0.91)
95% CI of LS mean	(-3.18, 0.38)	(-1.97, 1.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.21 (-1.31, 3.73)
Week 24 (MMRM)		
n	167	164
LS mean (SE)	93.13 (1.12)	92.24 (1.13)
95% CI of LS mean	(90.92, 95.35)	(90.01, 94.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.89 (-4.04, 2.25)
Absolute Change at Week 24 (MMRM)		
n	164	162
LS mean (SE)	-0.45 (0.88)	-0.39 (0.89)
95% CI of LS mean	(-2.18, 1.28)	(-2.14, 1.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-2.40, 2.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	94.21 (11.87)	93.08 (13.96)
Absolute Change at Week 52		
n	162	156
Mean (SD)	0.69 (10.19)	0.21 (10.29)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	93.89 (1.02)	92.81 (1.04)
95% CI of LS mean	(91.88, 95.90)	(90.77, 94.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.08 (-3.94, 1.79)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	0.33 (0.80)	0.22 (0.81)
95% CI of LS mean	(-1.23, 1.90)	(-1.37, 1.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-2.34, 2.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	-0.50 (0.66)	-0.12 (0.66)
95% CI of LS mean	(-1.80, 0.80)	(-1.43, 1.19)
P-value within Treatment	0.4458	0.8579
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.39 (-1.46, 2.23)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6814
Hedges' G (SE)		0.05 (0.11)
Hedges' 95% CI		(-0.17, 0.26)
Hedges' P-value		0.6813

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	92.40 (16.99)	88.19 (17.44)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	90.16 (4.26)	90.16 (4.65)
95% CI of LS mean	(81.47, 98.85)	(80.67, 99.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-13.06, 13.06)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	-1.72 (2.69)	1.35 (2.94)
95% CI of LS mean	(-7.21, 3.77)	(-4.65, 7.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.06 (-5.17, 11.30)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	86.65 (3.77)	88.77 (4.12)
95% CI of LS mean	(78.95, 94.34)	(80.36, 97.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.12 (-9.50, 13.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-5.23 (3.20)	-0.04 (3.49)
95% CI of LS mean	(-11.74, 1.28)	(-7.15, 7.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.18 (-4.54, 14.91)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	90.74 (4.03)	89.46 (4.40)
95% CI of LS mean	(82.51, 98.97)	(80.47, 98.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.28 (-13.67, 11.11)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	-1.13 (3.33)	0.65 (3.63)
95% CI of LS mean	(-7.91, 5.65)	(-6.75, 8.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.79 (-8.33, 11.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	94.44 (12.20)	91.27 (23.94)
Absolute Change at Week 52		
n	18	13
Mean (SD)	0.62 (8.92)	0.00 (15.04)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	92.99 (4.07)	90.49 (4.68)
95% CI of LS mean	(84.62, 101.35)	(80.92, 100.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.50 (-15.38, 10.38)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	0.59 (2.85)	0.42 (3.39)
95% CI of LS mean	(-5.27, 6.45)	(-6.53, 7.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-9.32, 8.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	-1.92 (2.30)	0.34 (2.55)
95% CI of LS mean	(-6.67, 2.83)	(-4.92, 5.61)
P-value within Treatment	0.4111	0.8945
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.27 (-4.93, 9.47)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5222
Hedges' G (SE)		0.22 (0.33)
Hedges' 95% CI		(-0.46, 0.90)
Hedges' P-value		0.5147

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	177	174
Mean (SD)	93.09 (13.91)	91.44 (16.48)
Week 8 (MMRM)		
n	178	172
LS mean (SE)	92.42 (1.19)	90.77 (1.21)
95% CI of LS mean	(90.07, 94.77)	(88.39, 93.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.65 (-5.00, 1.69)
Absolute Change at Week 8 (MMRM)		
n	174	170
LS mean (SE)	-0.85 (0.85)	-0.10 (0.86)
95% CI of LS mean	(-2.53, 0.83)	(-1.80, 1.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.75 (-1.64, 3.14)
Week 16 (MMRM)		
n	177	173
LS mean (SE)	92.21 (1.13)	90.82 (1.15)
95% CI of LS mean	(89.98, 94.44)	(88.56, 93.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.39 (-4.57, 1.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	173	170
LS mean (SE)	-1.16 (0.88)	-0.12 (0.89)
95% CI of LS mean	(-2.89, 0.57)	(-1.86, 1.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.04 (-1.41, 3.50)
Week 24 (MMRM)		
n	177	172
LS mean (SE)	93.06 (1.22)	90.43 (1.24)
95% CI of LS mean	(90.67, 95.46)	(88.00, 92.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.63 (-6.05, 0.78)
Absolute Change at Week 24 (MMRM)		
n	173	169
LS mean (SE)	-0.26 (0.84)	-0.52 (0.85)
95% CI of LS mean	(-1.90, 1.39)	(-2.19, 1.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.27 (-2.61, 2.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	174	169
Mean (SD)	93.61 (12.54)	91.19 (17.89)
Absolute Change at Week 52		
n	170	166
Mean (SD)	0.20 (9.93)	0.20 (11.89)
Week 52 (MMRM)		
n	173	167
LS mean (SE)	93.39 (1.13)	91.03 (1.15)
95% CI of LS mean	(91.17, 95.62)	(88.77, 93.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.37 (-5.54, 0.81)
Absolute Change at Week 52 (MMRM)		
n	169	164
LS mean (SE)	0.07 (0.85)	0.29 (0.86)
95% CI of LS mean	(-1.59, 1.74)	(-1.40, 1.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.22 (-2.15, 2.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	173	170
LS mean (SE)	-0.45 (0.68)	-0.12 (0.68)
95% CI of LS mean	(-1.78, 0.88)	(-1.46, 1.23)
P-value within Treatment	0.5080	0.8632
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.33 (-1.56, 2.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7315
Hedges' G (SE)		0.04 (0.11)
Hedges' 95% CI		(-0.17, 0.25)
Hedges' P-value		0.7314

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	114	115
Mean (SD)	92.98 (13.57)	92.85 (13.34)
Week 8 (MMRM)		
n	116	116
LS mean (SE)	91.56 (1.34)	92.87 (1.35)
95% CI of LS mean	(88.91, 94.21)	(90.21, 95.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.31 (-2.45, 5.06)
Absolute Change at Week 8 (MMRM)		
n	112	115
LS mean (SE)	-1.59 (1.08)	0.01 (1.06)
95% CI of LS mean	(-3.71, 0.53)	(-2.09, 2.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.59 (-1.39, 4.58)
Week 16 (MMRM)		
n	115	115
LS mean (SE)	91.93 (1.22)	92.54 (1.22)
95% CI of LS mean	(89.53, 94.34)	(90.13, 94.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.60 (-2.81, 4.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	111	114
LS mean (SE)	-1.44 (1.07)	-0.50 (1.06)
95% CI of LS mean	(-3.55, 0.67)	(-2.58, 1.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.94 (-2.03, 3.92)
Week 24 (MMRM)		
n	115	115
LS mean (SE)	92.34 (1.34)	92.45 (1.34)
95% CI of LS mean	(89.71, 94.98)	(89.81, 95.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.11 (-3.64, 3.85)
Absolute Change at Week 24 (MMRM)		
n	111	114
LS mean (SE)	-0.94 (1.05)	-0.58 (1.04)
95% CI of LS mean	(-3.02, 1.13)	(-2.63, 1.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-2.57, 3.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	113	111
Mean (SD)	94.10 (12.07)	93.19 (13.83)
Absolute Change at Week 52		
n	109	110
Mean (SD)	0.61 (9.42)	0.10 (11.41)
Week 52 (MMRM)		
n	112	111
LS mean (SE)	93.57 (1.22)	92.95 (1.23)
95% CI of LS mean	(91.16, 95.98)	(90.53, 95.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.62 (-4.04, 2.81)
Absolute Change at Week 52 (MMRM)		
n	108	110
LS mean (SE)	0.34 (1.01)	0.13 (1.00)
95% CI of LS mean	(-1.66, 2.34)	(-1.85, 2.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.21 (-3.02, 2.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	114
LS mean (SE)	-0.68 (0.81)	-0.32 (0.80)
95% CI of LS mean	(-2.28, 0.92)	(-1.89, 1.26)
P-value within Treatment	0.4016	0.6939
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.37 (-1.89, 2.62)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7497
Hedges' G (SE)		0.04 (0.13)
Hedges' 95% CI		(-0.22, 0.30)
Hedges' P-value		0.7488

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	77
Mean (SD)	92.64 (15.55)	88.46 (20.11)
Week 8 (MMRM)		
n	81	72
LS mean (SE)	92.39 (1.92)	88.34 (2.02)
95% CI of LS mean	(88.59, 96.18)	(84.35, 92.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.05 (-9.57, 1.47)
Absolute Change at Week 8 (MMRM)		
n	81	71
LS mean (SE)	-0.20 (1.22)	0.30 (1.30)
95% CI of LS mean	(-2.61, 2.21)	(-2.27, 2.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.49 (-3.03, 4.02)
Week 16 (MMRM)		
n	81	74
LS mean (SE)	90.60 (1.94)	88.58 (2.03)
95% CI of LS mean	(86.77, 94.43)	(84.57, 92.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.02 (-7.58, 3.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	81	72
LS mean (SE)	-1.94 (1.38)	0.68 (1.47)
95% CI of LS mean	(-4.67, 0.80)	(-2.22, 3.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.62 (-1.38, 6.61)
Week 24 (MMRM)		
n	81	73
LS mean (SE)	92.79 (2.01)	87.94 (2.11)
95% CI of LS mean	(88.81, 96.77)	(83.77, 92.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.85 (-10.62, 0.93)
Absolute Change at Week 24 (MMRM)		
n	81	71
LS mean (SE)	0.29 (1.31)	0.07 (1.40)
95% CI of LS mean	(-2.31, 2.88)	(-2.70, 2.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-4.02, 3.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	80	73
Mean (SD)	93.19 (13.05)	88.13 (23.30)
Absolute Change at Week 52		
n	80	70
Mean (SD)	0.28 (11.45)	0.48 (13.17)
Week 52 (MMRM)		
n	79	69
LS mean (SE)	92.27 (1.95)	88.77 (2.05)
95% CI of LS mean	(88.42, 96.11)	(84.71, 92.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.50 (-9.10, 2.10)
Absolute Change at Week 52 (MMRM)		
n	79	67
LS mean (SE)	-0.30 (1.34)	0.93 (1.44)
95% CI of LS mean	(-2.95, 2.34)	(-1.92, 3.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.24 (-2.66, 5.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	81	72
LS mean (SE)	-0.65 (1.09)	0.56 (1.16)
95% CI of LS mean	(-2.80, 1.50)	(-1.73, 2.85)
P-value within Treatment	0.5509	0.6299
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.21 (-1.94, 4.36)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4487
Hedges' G (SE)		0.12 (0.16)
Hedges' 95% CI		(-0.20, 0.44)
Hedges' P-value		0.4481

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	92.42 (16.03)	89.80 (15.92)
Week 8 (MMRM)		
n	88	83
LS mean (SE)	91.79 (1.92)	89.17 (1.97)
95% CI of LS mean	(88.00, 95.58)	(85.29, 93.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.62 (-8.05, 2.81)
Absolute Change at Week 8 (MMRM)		
n	86	82
LS mean (SE)	-1.33 (1.26)	0.14 (1.29)
95% CI of LS mean	(-3.81, 1.16)	(-2.40, 2.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.47 (-2.09, 5.03)
Week 16 (MMRM)		
n	89	85
LS mean (SE)	91.54 (1.69)	89.51 (1.73)
95% CI of LS mean	(88.20, 94.88)	(86.09, 92.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.03 (-6.81, 2.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	87	83
LS mean (SE)	-1.57 (1.19)	0.17 (1.22)
95% CI of LS mean	(-3.92, 0.79)	(-2.24, 2.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.73 (-1.64, 5.11)
Week 24 (MMRM)		
n	89	84
LS mean (SE)	90.67 (1.96)	89.23 (2.01)
95% CI of LS mean	(86.80, 94.54)	(85.26, 93.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.44 (-6.99, 4.11)
Absolute Change at Week 24 (MMRM)		
n	87	82
LS mean (SE)	-2.46 (1.33)	0.17 (1.37)
95% CI of LS mean	(-5.08, 0.16)	(-2.53, 2.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.63 (-1.13, 6.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	88	78
Mean (SD)	92.80 (14.20)	89.89 (18.63)
Absolute Change at Week 52		
n	86	76
Mean (SD)	0.26 (9.33)	0.58 (10.25)
Week 52 (MMRM)		
n	87	77
LS mean (SE)	93.05 (1.71)	89.18 (1.78)
95% CI of LS mean	(89.66, 96.43)	(85.67, 92.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.87 (-8.75, 1.01)
Absolute Change at Week 52 (MMRM)		
n	85	75
LS mean (SE)	-0.08 (1.00)	0.46 (1.06)
95% CI of LS mean	(-2.05, 1.90)	(-1.62, 2.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.54 (-2.33, 3.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	87	83
LS mean (SE)	-1.37 (0.88)	0.27 (0.91)
95% CI of LS mean	(-3.11, 0.37)	(-1.52, 2.06)
P-value within Treatment	0.1221	0.7672
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.64 (-0.86, 4.14)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1976
Hedges' G (SE)		0.20 (0.15)
Hedges' 95% CI		(-0.10, 0.50)
Hedges' P-value		0.1980

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	109	107
Mean (SD)	93.17 (13.00)	92.11 (16.93)
Week 8 (MMRM)		
n	109	105
LS mean (SE)	92.75 (1.39)	91.77 (1.41)
95% CI of LS mean	(90.02, 95.49)	(88.98, 94.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.98 (-4.89, 2.92)
Absolute Change at Week 8 (MMRM)		
n	107	104
LS mean (SE)	-0.52 (1.04)	-0.15 (1.06)
95% CI of LS mean	(-2.57, 1.54)	(-2.23, 1.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.37 (-2.56, 3.30)
Week 16 (MMRM)		
n	107	104
LS mean (SE)	91.96 (1.42)	91.36 (1.45)
95% CI of LS mean	(89.15, 94.76)	(88.51, 94.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.59 (-4.60, 3.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	105	103
LS mean (SE)	-1.47 (1.18)	-0.42 (1.19)
95% CI of LS mean	(-3.80, 0.86)	(-2.77, 1.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.05 (-2.26, 4.36)
Week 24 (MMRM)		
n	107	104
LS mean (SE)	94.85 (1.38)	91.05 (1.40)
95% CI of LS mean	(92.13, 97.56)	(88.29, 93.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.80 (-7.67, 0.07)
Absolute Change at Week 24 (MMRM)		
n	105	103
LS mean (SE)	1.51 (1.00)	-0.97 (1.01)
95% CI of LS mean	(-0.46, 3.47)	(-2.96, 1.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.48 (-5.27, 0.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	105	106
Mean (SD)	94.50 (10.80)	92.14 (18.08)
Absolute Change at Week 52		
n	103	104
Mean (SD)	0.65 (11.09)	0.00 (13.32)
Week 52 (MMRM)		
n	104	103
LS mean (SE)	93.72 (1.44)	92.12 (1.46)
95% CI of LS mean	(90.89, 96.56)	(89.25, 94.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.60 (-5.64, 2.43)
Absolute Change at Week 52 (MMRM)		
n	102	102
LS mean (SE)	0.32 (1.21)	0.14 (1.22)
95% CI of LS mean	(-2.07, 2.72)	(-2.27, 2.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-3.58, 3.21)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	105	103
LS mean (SE)	0.12 (0.92)	-0.42 (0.93)
95% CI of LS mean	(-1.70, 1.94)	(-2.26, 1.42)
P-value within Treatment	0.8974	0.6551
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.54 (-3.13, 2.05)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6832
Hedges' G (SE)		-0.06 (0.14)
Hedges' 95% CI		(-0.33, 0.22)
Hedges' P-value		0.6832

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	111	99
Mean (SD)	80.17 (19.50)	79.87 (19.49)
Week 8 (MMRM)		
n	113	98
LS mean (SE)	79.91 (1.67)	81.39 (1.79)
95% CI of LS mean	(76.62, 83.21)	(77.86, 84.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.48 (-3.37, 6.33)
Absolute Change at Week 8 (MMRM)		
n	110	96
LS mean (SE)	-0.64 (1.19)	1.67 (1.27)
95% CI of LS mean	(-2.99, 1.70)	(-0.84, 4.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.31 (-1.13, 5.76)
Week 16 (MMRM)		
n	113	98
LS mean (SE)	80.63 (1.74)	81.10 (1.87)
95% CI of LS mean	(77.20, 84.07)	(77.42, 84.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.47 (-4.58, 5.52)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	110	96
LS mean (SE)	0.14 (1.23)	1.49 (1.32)
95% CI of LS mean	(-2.28, 2.57)	(-1.11, 4.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.35 (-2.22, 4.91)
Week 24 (MMRM)		
n	113	98
LS mean (SE)	80.64 (1.67)	81.70 (1.79)
95% CI of LS mean	(77.35, 83.93)	(78.17, 85.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.06 (-3.78, 5.91)
Absolute Change at Week 24 (MMRM)		
n	110	96
LS mean (SE)	0.12 (1.37)	1.90 (1.47)
95% CI of LS mean	(-2.58, 2.83)	(-0.99, 4.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.78 (-2.19, 5.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	112	94
Mean (SD)	80.64 (18.68)	82.27 (17.01)
Absolute Change at Week 52		
n	109	92
Mean (SD)	-0.31 (13.16)	2.83 (14.26)
Week 52 (MMRM)		
n	112	93
LS mean (SE)	80.32 (1.69)	82.43 (1.83)
95% CI of LS mean	(76.98, 83.66)	(78.82, 86.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.11 (-2.82, 7.04)
Absolute Change at Week 52 (MMRM)		
n	109	91
LS mean (SE)	-0.20 (1.31)	2.52 (1.42)
95% CI of LS mean	(-2.78, 2.38)	(-0.27, 5.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.72 (-1.08, 6.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	110	96
LS mean (SE)	0.02 (1.14)	1.97 (1.23)
95% CI of LS mean	(-2.23, 2.28)	(-0.45, 4.39)
P-value within Treatment	0.9855	0.1096
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.95 (-1.37, 5.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2478
Hedges' G (SE)		0.16 (0.14)
Hedges' 95% CI		(-0.11, 0.44)
Hedges' P-value		0.2470

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	85	91
Mean (SD)	81.68 (16.76)	84.51 (14.73)
Week 8 (MMRM)		
n	84	90
LS mean (SE)	83.38 (1.73)	84.81 (1.67)
95% CI of LS mean	(79.96, 86.79)	(81.52, 88.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.44 (-3.31, 6.18)
Absolute Change at Week 8 (MMRM)		
n	83	90
LS mean (SE)	1.48 (1.02)	0.65 (0.98)
95% CI of LS mean	(-0.53, 3.50)	(-1.28, 2.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.83 (-3.63, 1.96)
Week 16 (MMRM)		
n	83	91
LS mean (SE)	83.56 (1.79)	84.01 (1.71)
95% CI of LS mean	(80.03, 87.09)	(80.63, 87.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-4.44, 5.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	82	90
LS mean (SE)	1.37 (1.28)	-0.12 (1.23)
95% CI of LS mean	(-1.17, 3.90)	(-2.54, 2.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.48 (-4.99, 2.02)
Week 24 (MMRM)		
n	83	90
LS mean (SE)	82.83 (1.81)	83.47 (1.73)
95% CI of LS mean	(79.26, 86.39)	(80.05, 86.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.64 (-4.30, 5.59)
Absolute Change at Week 24 (MMRM)		
n	82	89
LS mean (SE)	1.12 (1.31)	-0.74 (1.26)
95% CI of LS mean	(-1.47, 3.71)	(-3.22, 1.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.86 (-5.45, 1.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	80	87
Mean (SD)	81.94 (18.65)	83.38 (15.09)
Absolute Change at Week 52		
n	79	86
Mean (SD)	1.00 (12.18)	-0.47 (12.22)
Week 52 (MMRM)		
n	79	87
LS mean (SE)	82.51 (1.85)	83.88 (1.77)
95% CI of LS mean	(78.86, 86.15)	(80.39, 87.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.37 (-3.68, 6.43)
Absolute Change at Week 52 (MMRM)		
n	78	86
LS mean (SE)	0.67 (1.39)	-0.30 (1.33)
95% CI of LS mean	(-2.08, 3.41)	(-2.93, 2.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.97 (-4.77, 2.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	82	90
LS mean (SE)	1.05 (1.10)	-0.39 (1.05)
95% CI of LS mean	(-1.12, 3.22)	(-2.46, 1.69)
P-value within Treatment	0.3410	0.7142
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.44 (-4.44, 1.57)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3472
Hedges' G (SE)		-0.14 (0.15)
Hedges' 95% CI		(-0.44, 0.16)
Hedges' P-value		0.3474

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	29	25
Mean (SD)	77.76 (17.47)	86.03 (13.30)
Week 8 (MMRM)		
n	29	24
LS mean (SE)	82.03 (2.54)	84.81 (2.79)
95% CI of LS mean	(76.94, 87.13)	(79.21, 90.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.77 (-4.85, 10.39)
Absolute Change at Week 8 (MMRM)		
n	28	24
LS mean (SE)	3.87 (1.84)	0.35 (2.00)
95% CI of LS mean	(0.18, 7.56)	(-3.68, 4.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.52 (-9.01, 1.97)
Week 16 (MMRM)		
n	29	24
LS mean (SE)	83.46 (2.86)	82.48 (3.14)
95% CI of LS mean	(77.70, 89.21)	(76.17, 88.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.97 (-9.56, 7.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	28	23
LS mean (SE)	5.12 (2.14)	-1.78 (2.36)
95% CI of LS mean	(0.82, 9.42)	(-6.52, 2.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.90 (-13.32, -0.47)
Week 24 (MMRM)		
n	29	24
LS mean (SE)	84.90 (2.53)	84.59 (2.78)
95% CI of LS mean	(79.82, 89.98)	(79.01, 90.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-7.91, 7.30)
Absolute Change at Week 24 (MMRM)		
n	28	23
LS mean (SE)	6.68 (1.98)	0.04 (2.18)
95% CI of LS mean	(2.70, 10.66)	(-4.35, 4.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.64 (-12.59, -0.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	28	25
Mean (SD)	83.57 (15.30)	82.43 (17.05)
Absolute Change at Week 52		
n	27	24
Mean (SD)	5.12 (13.03)	-3.06 (12.60)
Week 52 (MMRM)		
n	28	24
LS mean (SE)	83.53 (3.03)	81.93 (3.31)
95% CI of LS mean	(77.46, 89.61)	(75.28, 88.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.60 (-10.65, 7.45)
Absolute Change at Week 52 (MMRM)		
n	27	23
LS mean (SE)	5.19 (2.49)	-2.77 (2.72)
95% CI of LS mean	(0.19, 10.19)	(-8.25, 2.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.96 (-15.40, -0.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	28	23
LS mean (SE)	5.66 (1.93)	-1.50 (2.13)
95% CI of LS mean	(1.78, 9.55)	(-5.78, 2.78)
P-value within Treatment	0.0052	0.4832
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.17 (-12.98, -1.36)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0166
Hedges' G (SE)		-0.69 (0.29)
Hedges' 95% CI		(-1.26, -0.12)
Hedges' P-value		0.0193

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	81.31 (18.43)	81.68 (17.96)
Week 8 (MMRM)		
n	168	164
LS mean (SE)	81.29 (1.34)	82.74 (1.36)
95% CI of LS mean	(78.65, 83.93)	(80.07, 85.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.45 (-2.31, 5.20)
Absolute Change at Week 8 (MMRM)		
n	165	162
LS mean (SE)	-0.45 (0.88)	1.38 (0.89)
95% CI of LS mean	(-2.18, 1.28)	(-0.37, 3.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.83 (-0.63, 4.29)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	81.64 (1.39)	82.48 (1.40)
95% CI of LS mean	(78.91, 84.37)	(79.73, 85.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.84 (-3.04, 4.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	-0.17 (0.98)	1.16 (0.98)
95% CI of LS mean	(-2.09, 1.75)	(-0.77, 3.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.33 (-1.39, 4.05)
Week 24 (MMRM)		
n	167	164
LS mean (SE)	81.00 (1.36)	82.23 (1.38)
95% CI of LS mean	(78.32, 83.69)	(79.53, 84.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.23 (-2.58, 5.04)
Absolute Change at Week 24 (MMRM)		
n	164	162
LS mean (SE)	-0.58 (1.07)	0.81 (1.07)
95% CI of LS mean	(-2.68, 1.52)	(-1.30, 2.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.39 (-1.59, 4.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	80.85 (19.12)	82.98 (15.92)
Absolute Change at Week 52		
n	162	156
Mean (SD)	-0.45 (12.61)	1.88 (13.33)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	80.85 (1.36)	83.34 (1.38)
95% CI of LS mean	(78.17, 83.53)	(80.62, 86.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.49 (-1.33, 6.31)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	-0.80 (1.02)	1.86 (1.04)
95% CI of LS mean	(-2.81, 1.21)	(-0.18, 3.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.66 (-0.20, 5.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	-0.52 (0.87)	1.27 (0.88)
95% CI of LS mean	(-2.24, 1.20)	(-0.45, 3.00)
P-value within Treatment	0.5530	0.1479
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.79 (-0.65, 4.23)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1490
Hedges' G (SE)		0.16 (0.11)
Hedges' 95% CI		(-0.06, 0.38)
Hedges' P-value		0.1494

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	82.11 (17.51)	75.83 (23.71)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	84.08 (4.37)	80.99 (4.77)
95% CI of LS mean	(75.19, 92.97)	(71.27, 90.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.09 (-16.43, 10.25)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	1.42 (3.14)	5.81 (3.43)
95% CI of LS mean	(-4.98, 7.83)	(-1.19, 12.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.38 (-5.28, 14.05)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	84.08 (3.31)	77.66 (3.62)
95% CI of LS mean	(77.33, 90.83)	(70.27, 85.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.42 (-16.66, 3.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	1.42 (3.41)	2.47 (3.73)
95% CI of LS mean	(-5.53, 8.38)	(-5.13, 10.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.05 (-9.41, 11.51)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	87.59 (3.94)	76.82 (4.30)
95% CI of LS mean	(79.55, 95.63)	(68.04, 85.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-10.77 (-22.86, 1.32)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	4.93 (4.30)	1.64 (4.69)
95% CI of LS mean	(-3.81, 13.68)	(-7.91, 11.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.29 (-16.36, 9.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	83.70 (21.60)	76.67 (15.41)
Absolute Change at Week 52		
n	18	13
Mean (SD)	1.11 (16.37)	3.59 (17.77)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	83.76 (4.76)	77.54 (5.47)
95% CI of LS mean	(74.03, 93.50)	(66.39, 88.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.22 (-21.17, 8.73)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	1.09 (3.87)	2.36 (4.52)
95% CI of LS mean	(-6.86, 9.04)	(-6.90, 11.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.26 (-11.05, 13.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	2.48 (3.33)	2.16 (3.68)
95% CI of LS mean	(-4.31, 9.28)	(-5.34, 9.65)
P-value within Treatment	0.4613	0.5616
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-10.60, 9.94)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9488
Hedges' G (SE)		-0.02 (0.33)
Hedges' 95% CI		(-0.70, 0.65)
Hedges' P-value		0.9479

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	177	174
Mean (SD)	80.80 (18.35)	82.86 (16.70)
Week 8 (MMRM)		
n	178	172
LS mean (SE)	81.27 (1.25)	83.07 (1.27)
95% CI of LS mean	(78.82, 83.73)	(80.58, 85.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.80 (-1.70, 5.30)
Absolute Change at Week 8 (MMRM)		
n	174	170
LS mean (SE)	0.10 (0.83)	0.80 (0.84)
95% CI of LS mean	(-1.53, 1.72)	(-0.85, 2.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.70 (-1.61, 3.02)
Week 16 (MMRM)		
n	177	173
LS mean (SE)	81.81 (1.34)	82.79 (1.35)
95% CI of LS mean	(79.18, 84.43)	(80.13, 85.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.99 (-2.75, 4.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	173	170
LS mean (SE)	0.53 (0.93)	0.61 (0.94)
95% CI of LS mean	(-1.29, 2.35)	(-1.23, 2.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-2.51, 2.67)
Week 24 (MMRM)		
n	177	172
LS mean (SE)	81.07 (1.29)	82.94 (1.30)
95% CI of LS mean	(78.54, 83.60)	(80.37, 85.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.87 (-1.74, 5.47)
Absolute Change at Week 24 (MMRM)		
n	173	169
LS mean (SE)	0.01 (0.97)	0.60 (0.98)
95% CI of LS mean	(-1.89, 1.91)	(-1.32, 2.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.59 (-2.12, 3.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	174	169
Mean (SD)	81.15 (18.25)	83.48 (16.05)
Absolute Change at Week 52		
n	170	166
Mean (SD)	0.26 (12.45)	0.96 (12.95)
Week 52 (MMRM)		
n	173	167
LS mean (SE)	81.07 (1.30)	83.53 (1.32)
95% CI of LS mean	(78.52, 83.62)	(80.95, 86.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.46 (-1.17, 6.10)
Absolute Change at Week 52 (MMRM)		
n	169	164
LS mean (SE)	-0.05 (0.98)	1.15 (0.99)
95% CI of LS mean	(-1.97, 1.87)	(-0.80, 3.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.19 (-1.54, 3.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	173	170
LS mean (SE)	0.17 (0.82)	0.78 (0.83)
95% CI of LS mean	(-1.45, 1.78)	(-0.85, 2.42)
P-value within Treatment	0.8405	0.3454
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.62 (-1.68, 2.92)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5966
Hedges' G (SE)		0.06 (0.11)
Hedges' 95% CI		(-0.15, 0.27)
Hedges' P-value		0.5965

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	114	115
Mean (SD)	81.77 (18.84)	82.10 (17.95)
Week 8 (MMRM)		
n	116	116
LS mean (SE)	81.60 (1.57)	83.97 (1.58)
95% CI of LS mean	(78.50, 84.70)	(80.86, 87.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-2.03, 6.79)
Absolute Change at Week 8 (MMRM)		
n	112	115
LS mean (SE)	-0.72 (1.13)	2.10 (1.11)
95% CI of LS mean	(-2.94, 1.51)	(-0.10, 4.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.82 (-0.32, 5.95)
Week 16 (MMRM)		
n	115	115
LS mean (SE)	82.77 (1.69)	83.12 (1.69)
95% CI of LS mean	(79.44, 86.10)	(79.78, 86.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.35 (-4.38, 5.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	111	114
LS mean (SE)	0.41 (1.21)	1.34 (1.20)
95% CI of LS mean	(-1.99, 2.80)	(-1.03, 3.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (-2.44, 4.30)
Week 24 (MMRM)		
n	115	115
LS mean (SE)	81.30 (1.70)	82.25 (1.70)
95% CI of LS mean	(77.95, 84.65)	(78.89, 85.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.95 (-3.81, 5.71)
Absolute Change at Week 24 (MMRM)		
n	111	114
LS mean (SE)	-0.76 (1.31)	0.40 (1.30)
95% CI of LS mean	(-3.34, 1.82)	(-2.15, 2.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.16 (-2.48, 4.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	113	111
Mean (SD)	81.67 (17.78)	83.42 (16.55)
Absolute Change at Week 52		
n	109	110
Mean (SD)	-0.36 (11.70)	1.64 (12.62)
Week 52 (MMRM)		
n	112	111
LS mean (SE)	81.19 (1.61)	83.66 (1.61)
95% CI of LS mean	(78.02, 84.36)	(80.48, 86.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.48 (-2.03, 6.98)
Absolute Change at Week 52 (MMRM)		
n	108	110
LS mean (SE)	-0.97 (1.17)	1.75 (1.16)
95% CI of LS mean	(-3.28, 1.33)	(-0.53, 4.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.73 (-0.52, 5.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	114
LS mean (SE)	-0.44 (1.08)	1.16 (1.07)
95% CI of LS mean	(-2.57, 1.69)	(-0.94, 3.27)
P-value within Treatment	0.6831	0.2774
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.61 (-1.40, 4.61)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2937
Hedges' G (SE)		0.14 (0.13)
Hedges' 95% CI		(-0.12, 0.40)
Hedges' P-value		0.2926

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	77
Mean (SD)	79.44 (17.54)	82.46 (16.82)
Week 8 (MMRM)		
n	81	72
LS mean (SE)	81.11 (1.90)	81.53 (1.99)
95% CI of LS mean	(77.36, 84.86)	(77.59, 85.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.42 (-5.03, 5.86)
Absolute Change at Week 8 (MMRM)		
n	81	71
LS mean (SE)	1.33 (1.09)	0.04 (1.17)
95% CI of LS mean	(-0.84, 3.49)	(-2.27, 2.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.29 (-4.46, 1.88)
Week 16 (MMRM)		
n	81	74
LS mean (SE)	80.57 (1.86)	81.60 (1.95)
95% CI of LS mean	(76.88, 84.25)	(77.74, 85.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.03 (-4.31, 6.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	81	72
LS mean (SE)	0.71 (1.30)	0.07 (1.37)
95% CI of LS mean	(-1.85, 3.27)	(-2.65, 2.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-4.38, 3.10)
Week 24 (MMRM)		
n	81	73
LS mean (SE)	81.85 (1.73)	83.09 (1.82)
95% CI of LS mean	(78.43, 85.27)	(79.50, 86.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.24 (-3.74, 6.21)
Absolute Change at Week 24 (MMRM)		
n	81	71
LS mean (SE)	2.03 (1.39)	1.36 (1.48)
95% CI of LS mean	(-0.71, 4.77)	(-1.56, 4.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.67 (-4.68, 3.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	80	73
Mean (SD)	80.64 (19.80)	82.11 (15.29)
Absolute Change at Week 52		
n	80	70
Mean (SD)	1.30 (14.16)	0.57 (14.39)
Week 52 (MMRM)		
n	79	69
LS mean (SE)	81.12 (2.00)	82.41 (2.11)
95% CI of LS mean	(77.18, 85.07)	(78.24, 86.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.29 (-4.46, 7.04)
Absolute Change at Week 52 (MMRM)		
n	79	67
LS mean (SE)	1.31 (1.62)	0.62 (1.75)
95% CI of LS mean	(-1.89, 4.52)	(-2.83, 4.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.69 (-5.41, 4.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	81	72
LS mean (SE)	1.35 (1.20)	0.68 (1.28)
95% CI of LS mean	(-1.02, 3.72)	(-1.84, 3.21)
P-value within Treatment	0.2627	0.5941
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.67 (-4.14, 2.80)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7047
Hedges' G (SE)		-0.06 (0.16)
Hedges' 95% CI		(-0.38, 0.26)
Hedges' P-value		0.7042

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	82.23 (17.24)	82.37 (17.56)
Week 8 (MMRM)		
n	88	83
LS mean (SE)	81.93 (1.79)	82.61 (1.84)
95% CI of LS mean	(78.39, 85.47)	(78.98, 86.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.68 (-4.39, 5.76)
Absolute Change at Week 8 (MMRM)		
n	86	82
LS mean (SE)	-0.71 (1.21)	0.74 (1.24)
95% CI of LS mean	(-3.11, 1.68)	(-1.71, 3.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.46 (-1.98, 4.89)
Week 16 (MMRM)		
n	89	85
LS mean (SE)	84.05 (1.90)	81.07 (1.94)
95% CI of LS mean	(80.31, 87.80)	(77.24, 84.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.99 (-8.35, 2.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	87	83
LS mean (SE)	1.19 (1.35)	-0.48 (1.39)
95% CI of LS mean	(-1.48, 3.87)	(-3.21, 2.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.67 (-5.50, 2.15)
Week 24 (MMRM)		
n	89	84
LS mean (SE)	82.62 (1.93)	81.39 (1.98)
95% CI of LS mean	(78.81, 86.44)	(77.47, 85.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.24 (-6.71, 4.24)
Absolute Change at Week 24 (MMRM)		
n	87	82
LS mean (SE)	0.19 (1.50)	-0.32 (1.54)
95% CI of LS mean	(-2.77, 3.15)	(-3.36, 2.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.51 (-4.76, 3.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	88	78
Mean (SD)	82.34 (17.21)	81.91 (18.12)
Absolute Change at Week 52		
n	86	76
Mean (SD)	0.27 (10.46)	0.56 (13.00)
Week 52 (MMRM)		
n	87	77
LS mean (SE)	82.86 (1.87)	82.44 (1.93)
95% CI of LS mean	(79.17, 86.54)	(78.63, 86.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.42 (-5.73, 4.88)
Absolute Change at Week 52 (MMRM)		
n	85	75
LS mean (SE)	0.28 (1.27)	0.58 (1.33)
95% CI of LS mean	(-2.24, 2.79)	(-2.04, 3.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.31 (-3.34, 3.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	87	83
LS mean (SE)	0.55 (1.20)	-0.07 (1.23)
95% CI of LS mean	(-1.82, 2.92)	(-2.50, 2.36)
P-value within Treatment	0.6450	0.9538
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.63 (-4.03, 2.78)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7171
Hedges' G (SE)		-0.06 (0.15)
Hedges' 95% CI		(-0.36, 0.25)
Hedges' P-value		0.7167

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	109	107
Mean (SD)	79.63 (19.10)	82.14 (17.46)
Week 8 (MMRM)		
n	109	105
LS mean (SE)	81.12 (1.63)	83.24 (1.66)
95% CI of LS mean	(77.91, 84.33)	(79.96, 86.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.12 (-2.47, 6.70)
Absolute Change at Week 8 (MMRM)		
n	107	104
LS mean (SE)	0.97 (1.07)	1.62 (1.09)
95% CI of LS mean	(-1.14, 3.08)	(-0.52, 3.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.65 (-2.36, 3.66)
Week 16 (MMRM)		
n	107	104
LS mean (SE)	80.27 (1.66)	83.49 (1.69)
95% CI of LS mean	(76.99, 83.55)	(80.16, 86.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.22 (-1.46, 7.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	105	103
LS mean (SE)	0.13 (1.19)	1.76 (1.21)
95% CI of LS mean	(-2.22, 2.49)	(-0.62, 4.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.63 (-1.72, 4.98)
Week 24 (MMRM)		
n	107	104
LS mean (SE)	80.87 (1.57)	83.34 (1.60)
95% CI of LS mean	(77.77, 83.96)	(80.19, 86.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.47 (-1.95, 6.88)
Absolute Change at Week 24 (MMRM)		
n	105	103
LS mean (SE)	0.75 (1.26)	1.48 (1.27)
95% CI of LS mean	(-1.73, 3.22)	(-1.03, 3.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.73 (-2.79, 4.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	105	106
Mean (SD)	80.33 (19.73)	83.63 (14.35)
Absolute Change at Week 52		
n	103	104
Mean (SD)	0.40 (14.50)	1.71 (13.57)
Week 52 (MMRM)		
n	104	103
LS mean (SE)	80.01 (1.67)	83.65 (1.70)
95% CI of LS mean	(76.71, 83.31)	(80.31, 87.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.64 (-1.06, 8.34)
Absolute Change at Week 52 (MMRM)		
n	102	102
LS mean (SE)	-0.13 (1.39)	1.81 (1.40)
95% CI of LS mean	(-2.87, 2.61)	(-0.94, 4.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.94 (-1.95, 5.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	105	103
LS mean (SE)	0.25 (1.09)	1.68 (1.10)
95% CI of LS mean	(-1.90, 2.41)	(-0.49, 3.86)
P-value within Treatment	0.8188	0.1286
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.43 (-1.63, 4.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3571
Hedges' G (SE)		0.13 (0.14)
Hedges' 95% CI		(-0.15, 0.40)
Hedges' P-value		0.3575

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	108	99
Mean (SD)	69.03 (20.50)	71.38 (21.30)
Week 8 (MMRM)		
n	109	98
LS mean (SE)	66.74 (2.02)	69.77 (2.13)
95% CI of LS mean	(62.77, 70.72)	(65.58, 73.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.03 (-2.76, 8.82)
Absolute Change at Week 8 (MMRM)		
n	107	96
LS mean (SE)	-2.17 (1.45)	-2.02 (1.53)
95% CI of LS mean	(-5.02, 0.68)	(-5.03, 0.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-4.01, 4.30)
Week 16 (MMRM)		
n	109	98
LS mean (SE)	68.28 (2.00)	70.37 (2.11)
95% CI of LS mean	(64.33, 72.23)	(66.21, 74.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.10 (-3.66, 7.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	107	96
LS mean (SE)	-0.75 (1.40)	-1.28 (1.48)
95% CI of LS mean	(-3.50, 2.01)	(-4.20, 1.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.54 (-4.56, 3.48)
Week 24 (MMRM)		
n	109	98
LS mean (SE)	68.56 (2.05)	70.51 (2.16)
95% CI of LS mean	(64.51, 72.60)	(66.24, 74.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.95 (-3.94, 7.84)
Absolute Change at Week 24 (MMRM)		
n	107	96
LS mean (SE)	-0.43 (1.28)	-1.63 (1.35)
95% CI of LS mean	(-2.96, 2.09)	(-4.30, 1.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.20 (-4.87, 2.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	108	94
Mean (SD)	70.27 (20.87)	71.99 (21.72)
Absolute Change at Week 52		
n	106	92
Mean (SD)	0.42 (12.64)	0.48 (15.88)
Week 52 (MMRM)		
n	108	93
LS mean (SE)	69.65 (2.03)	72.50 (2.15)
95% CI of LS mean	(65.66, 73.65)	(68.25, 76.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.84 (-3.00, 8.69)
Absolute Change at Week 52 (MMRM)		
n	106	91
LS mean (SE)	0.55 (1.39)	0.31 (1.49)
95% CI of LS mean	(-2.20, 3.29)	(-2.63, 3.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-4.27, 3.79)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	107	96
LS mean (SE)	-0.21 (1.09)	-0.87 (1.15)
95% CI of LS mean	(-2.36, 1.93)	(-3.14, 1.40)
P-value within Treatment	0.8464	0.4521
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.66 (-3.79, 2.48)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6797
Hedges' G (SE)		-0.06 (0.14)
Hedges' 95% CI		(-0.33, 0.22)
Hedges' P-value		0.6788

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	80	86
Mean (SD)	74.17 (17.12)	76.36 (16.94)
Week 8 (MMRM)		
n	80	85
LS mean (SE)	75.06 (1.84)	77.00 (1.78)
95% CI of LS mean	(71.42, 78.70)	(73.48, 80.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.94 (-3.13, 7.01)
Absolute Change at Week 8 (MMRM)		
n	79	85
LS mean (SE)	0.65 (1.44)	0.66 (1.39)
95% CI of LS mean	(-2.20, 3.49)	(-2.08, 3.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.02 (-3.94, 3.97)
Week 16 (MMRM)		
n	78	86
LS mean (SE)	75.37 (2.11)	75.98 (2.02)
95% CI of LS mean	(71.19, 79.54)	(71.98, 79.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.61 (-5.17, 6.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	77	86
LS mean (SE)	0.44 (1.64)	-0.40 (1.55)
95% CI of LS mean	(-2.79, 3.67)	(-3.47, 2.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.84 (-5.29, 3.62)
Week 24 (MMRM)		
n	78	85
LS mean (SE)	72.36 (2.16)	78.49 (2.08)
95% CI of LS mean	(68.08, 76.63)	(74.38, 82.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.13 (0.20, 12.06)
Absolute Change at Week 24 (MMRM)		
n	77	85
LS mean (SE)	-2.35 (1.71)	2.14 (1.63)
95% CI of LS mean	(-5.73, 1.03)	(-1.07, 5.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.50 (-0.17, 9.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	75	82
Mean (SD)	76.37 (18.18)	78.32 (17.62)
Absolute Change at Week 52		
n	74	82
Mean (SD)	2.33 (13.33)	2.03 (13.98)
Week 52 (MMRM)		
n	74	82
LS mean (SE)	77.43 (2.00)	78.61 (1.91)
95% CI of LS mean	(73.48, 81.39)	(74.83, 82.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-4.30, 6.64)
Absolute Change at Week 52 (MMRM)		
n	73	82
LS mean (SE)	2.83 (1.59)	2.20 (1.50)
95% CI of LS mean	(-0.32, 5.97)	(-0.77, 5.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.63 (-4.95, 3.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	77	86
LS mean (SE)	0.30 (1.30)	1.31 (1.23)
95% CI of LS mean	(-2.26, 2.87)	(-1.12, 3.75)
P-value within Treatment	0.8158	0.2881
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.01 (-2.53, 4.55)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5732
Hedges' G (SE)		0.09 (0.16)
Hedges' 95% CI		(-0.22, 0.40)
Hedges' P-value		0.5732

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	21	20
Mean (SD)	71.43 (13.87)	81.67 (14.98)
Week 8 (MMRM)		
n	21	19
LS mean (SE)	73.22 (3.56)	78.72 (3.74)
95% CI of LS mean	(66.00, 80.44)	(71.13, 86.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.50 (-5.01, 16.01)
Absolute Change at Week 8 (MMRM)		
n	21	19
LS mean (SE)	2.03 (2.81)	-2.25 (2.95)
95% CI of LS mean	(-3.66, 7.72)	(-8.23, 3.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.28 (-12.56, 4.00)
Week 16 (MMRM)		
n	20	19
LS mean (SE)	72.28 (3.77)	74.63 (3.91)
95% CI of LS mean	(64.63, 79.94)	(66.69, 82.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.35 (-8.71, 13.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	20	19
LS mean (SE)	1.00 (3.03)	-6.34 (3.12)
95% CI of LS mean	(-5.13, 7.14)	(-12.67, -0.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.34 (-16.18, 1.49)
Week 24 (MMRM)		
n	20	19
LS mean (SE)	69.13 (4.31)	76.97 (4.44)
95% CI of LS mean	(60.38, 77.88)	(67.97, 85.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.84 (-4.75, 20.42)
Absolute Change at Week 24 (MMRM)		
n	20	19
LS mean (SE)	-2.09 (3.94)	-4.00 (4.04)
95% CI of LS mean	(-10.08, 5.90)	(-12.19, 4.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.91 (-13.37, 9.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	19	20
Mean (SD)	74.27 (17.78)	79.44 (15.41)
Absolute Change at Week 52		
n	19	20
Mean (SD)	2.92 (12.75)	-2.22 (15.12)
Week 52 (MMRM)		
n	19	19
LS mean (SE)	74.57 (3.78)	78.72 (3.82)
95% CI of LS mean	(66.91, 82.23)	(70.97, 86.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.16 (-6.77, 15.09)
Absolute Change at Week 52 (MMRM)		
n	19	19
LS mean (SE)	3.25 (3.31)	-2.25 (3.31)
95% CI of LS mean	(-3.45, 9.95)	(-8.96, 4.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.50 (-15.00, 4.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	20	19
LS mean (SE)	0.72 (2.30)	-4.20 (2.35)
95% CI of LS mean	(-3.94, 5.38)	(-8.97, 0.58)
P-value within Treatment	0.7555	0.0832
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.92 (-11.62, 1.78)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1452
Hedges' G (SE)		-0.47 (0.32)
Hedges' 95% CI		(-1.11, 0.18)
Hedges' P-value		0.1487

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	71.10 (19.84)	72.99 (19.83)
Week 8 (MMRM)		
n	168	164
LS mean (SE)	70.04 (1.49)	72.34 (1.51)
95% CI of LS mean	(67.11, 72.97)	(69.38, 75.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.30 (-1.87, 6.47)
Absolute Change at Week 8 (MMRM)		
n	165	162
LS mean (SE)	-1.43 (1.10)	-0.51 (1.11)
95% CI of LS mean	(-3.61, 0.74)	(-2.71, 1.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.92 (-2.17, 4.01)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	71.26 (1.57)	72.64 (1.58)
95% CI of LS mean	(68.17, 74.34)	(69.53, 75.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.38 (-3.00, 5.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	-0.47 (1.13)	-0.15 (1.13)
95% CI of LS mean	(-2.69, 1.74)	(-2.37, 2.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.33 (-2.81, 3.46)
Week 24 (MMRM)		
n	167	164
LS mean (SE)	70.38 (1.59)	73.74 (1.61)
95% CI of LS mean	(67.24, 73.52)	(70.57, 76.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.36 (-1.10, 7.81)
Absolute Change at Week 24 (MMRM)		
n	164	162
LS mean (SE)	-1.22 (1.07)	0.70 (1.07)
95% CI of LS mean	(-3.32, 0.88)	(-1.41, 2.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.92 (-1.06, 4.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	72.49 (20.25)	74.42 (20.53)
Absolute Change at Week 52		
n	162	156
Mean (SD)	0.99 (12.93)	1.50 (14.99)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	72.78 (1.55)	74.80 (1.57)
95% CI of LS mean	(69.74, 75.82)	(71.72, 77.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.02 (-2.31, 6.36)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	1.15 (1.10)	1.70 (1.12)
95% CI of LS mean	(-1.02, 3.32)	(-0.50, 3.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.55 (-2.54, 3.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	-0.18 (0.89)	0.75 (0.89)
95% CI of LS mean	(-1.93, 1.57)	(-1.01, 2.51)
P-value within Treatment	0.8400	0.4020
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (-1.55, 3.41)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4615
Hedges' G (SE)		0.08 (0.11)
Hedges' 95% CI		(-0.14, 0.30)
Hedges' P-value		0.4615

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	71.93 (20.41)	67.36 (24.50)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	67.88 (4.49)	71.48 (4.91)
95% CI of LS mean	(58.71, 77.05)	(61.45, 81.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.60 (-10.23, 17.42)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	-4.43 (3.10)	4.57 (3.39)
95% CI of LS mean	(-10.76, 1.90)	(-2.34, 11.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.01 (-0.47, 18.48)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	66.71 (4.14)	71.48 (4.53)
95% CI of LS mean	(58.26, 75.16)	(62.23, 80.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.77 (-8.02, 17.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-5.60 (3.86)	4.57 (4.21)
95% CI of LS mean	(-13.49, 2.28)	(-4.03, 13.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.18 (-1.57, 21.92)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	63.79 (4.87)	69.39 (5.32)
95% CI of LS mean	(53.86, 73.71)	(58.55, 80.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.61 (-9.31, 20.52)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	-8.53 (4.55)	2.49 (4.96)
95% CI of LS mean	(-17.81, 0.76)	(-7.64, 12.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.02 (-2.79, 24.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	74.07 (22.55)	66.67 (22.22)
Absolute Change at Week 52		
n	18	13
Mean (SD)	1.85 (10.26)	1.71 (12.71)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	73.64 (4.98)	67.84 (5.71)
95% CI of LS mean	(63.42, 83.86)	(56.18, 79.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.80 (-21.49, 9.89)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	1.33 (2.56)	2.31 (3.03)
95% CI of LS mean	(-3.91, 6.57)	(-3.89, 8.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.98 (-7.21, 9.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	-4.27 (2.87)	3.12 (3.16)
95% CI of LS mean	(-10.15, 1.61)	(-3.34, 9.59)
P-value within Treatment	0.1481	0.3308
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.39 (-1.44, 16.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0976
Hedges' G (SE)		0.58 (0.34)
Hedges' 95% CI		(-0.11, 1.26)
Hedges' P-value		0.0989

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	169	169
Mean (SD)	71.20 (19.11)	74.62 (18.91)
Week 8 (MMRM)		
n	170	167
LS mean (SE)	70.69 (1.45)	73.13 (1.46)
95% CI of LS mean	(67.84, 73.55)	(70.25, 76.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.44 (-1.62, 6.49)
Absolute Change at Week 8 (MMRM)		
n	167	165
LS mean (SE)	-0.75 (1.09)	-1.11 (1.10)
95% CI of LS mean	(-2.90, 1.41)	(-3.28, 1.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.37 (-3.42, 2.68)
Week 16 (MMRM)		
n	168	168
LS mean (SE)	71.92 (1.55)	72.96 (1.55)
95% CI of LS mean	(68.87, 74.96)	(69.91, 76.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.04 (-3.27, 5.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	165	166
LS mean (SE)	0.19 (1.11)	-1.22 (1.10)
95% CI of LS mean	(-1.99, 2.36)	(-3.39, 0.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.41 (-4.49, 1.66)
Week 24 (MMRM)		
n	168	167
LS mean (SE)	71.05 (1.57)	74.50 (1.58)
95% CI of LS mean	(67.96, 74.15)	(71.40, 77.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.44 (-0.94, 7.83)
Absolute Change at Week 24 (MMRM)		
n	165	165
LS mean (SE)	-0.56 (1.05)	0.08 (1.05)
95% CI of LS mean	(-2.63, 1.51)	(-1.99, 2.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.64 (-2.29, 3.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	165	164
Mean (SD)	72.83 (19.41)	75.88 (19.68)
Absolute Change at Week 52		
n	162	162
Mean (SD)	1.27 (13.08)	1.03 (15.26)
Week 52 (MMRM)		
n	164	162
LS mean (SE)	72.96 (1.51)	75.84 (1.51)
95% CI of LS mean	(70.00, 75.93)	(72.86, 78.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.88 (-1.33, 7.08)
Absolute Change at Week 52 (MMRM)		
n	161	160
LS mean (SE)	1.33 (1.12)	1.33 (1.12)
95% CI of LS mean	(-0.87, 3.54)	(-0.88, 3.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-3.12, 3.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	165	166
LS mean (SE)	0.32 (0.88)	0.06 (0.88)
95% CI of LS mean	(-1.40, 2.04)	(-1.66, 1.79)
P-value within Treatment	0.7148	0.9431
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-2.70, 2.18)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8353
Hedges' G (SE)		-0.02 (0.11)
Hedges' 95% CI		(-0.24, 0.19)
Hedges' P-value		0.8352

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	109	114
Mean (SD)	71.36 (20.25)	73.78 (20.96)
Week 8 (MMRM)		
n	110	115
LS mean (SE)	69.96 (1.89)	74.24 (1.86)
95% CI of LS mean	(66.23, 73.69)	(70.58, 77.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.28 (-0.96, 9.51)
Absolute Change at Week 8 (MMRM)		
n	107	114
LS mean (SE)	-1.62 (1.37)	0.52 (1.33)
95% CI of LS mean	(-4.32, 1.08)	(-2.09, 3.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.15 (-1.62, 5.91)
Week 16 (MMRM)		
n	109	115
LS mean (SE)	72.24 (1.97)	73.17 (1.93)
95% CI of LS mean	(68.35, 76.13)	(69.37, 76.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (-4.51, 6.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	106	114
LS mean (SE)	0.29 (1.33)	-0.55 (1.28)
95% CI of LS mean	(-2.33, 2.91)	(-3.08, 1.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.83 (-4.48, 2.81)
Week 24 (MMRM)		
n	109	115
LS mean (SE)	71.00 (2.00)	74.24 (1.96)
95% CI of LS mean	(67.05, 74.95)	(70.38, 78.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.24 (-2.29, 8.77)
Absolute Change at Week 24 (MMRM)		
n	106	114
LS mean (SE)	-0.76 (1.23)	0.52 (1.19)
95% CI of LS mean	(-3.19, 1.66)	(-1.82, 2.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.29 (-2.09, 4.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	107	111
Mean (SD)	73.57 (19.15)	74.07 (21.52)
Absolute Change at Week 52		
n	104	110
Mean (SD)	1.44 (10.98)	0.30 (14.71)
Week 52 (MMRM)		
n	106	111
LS mean (SE)	73.28 (1.95)	74.19 (1.91)
95% CI of LS mean	(69.44, 77.12)	(70.43, 77.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.91 (-4.47, 6.30)
Absolute Change at Week 52 (MMRM)		
n	103	110
LS mean (SE)	1.47 (1.28)	0.36 (1.24)
95% CI of LS mean	(-1.05, 3.99)	(-2.08, 2.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.11 (-4.62, 2.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	106	114
LS mean (SE)	0.33 (1.04)	0.11 (1.00)
95% CI of LS mean	(-1.71, 2.37)	(-1.86, 2.09)
P-value within Treatment	0.7504	0.9109
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-3.06, 2.63)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8801
Hedges' G (SE)		-0.02 (0.13)
Hedges' 95% CI		(-0.29, 0.24)
Hedges' P-value		0.8799

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	80	73
Mean (SD)	70.83 (17.89)	74.12 (17.18)
Week 8 (MMRM)		
n	79	68
LS mean (SE)	71.06 (2.00)	70.83 (2.14)
95% CI of LS mean	(67.11, 75.01)	(66.61, 75.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-6.02, 5.55)
Absolute Change at Week 8 (MMRM)		
n	79	67
LS mean (SE)	-0.30 (1.55)	-2.71 (1.67)
95% CI of LS mean	(-3.36, 2.76)	(-6.02, 0.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.42 (-6.93, 2.09)
Week 16 (MMRM)		
n	78	69
LS mean (SE)	70.27 (2.17)	72.24 (2.30)
95% CI of LS mean	(65.99, 74.55)	(67.69, 76.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.97 (-4.29, 8.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	78	68
LS mean (SE)	-1.14 (1.75)	-1.09 (1.88)
95% CI of LS mean	(-4.61, 2.33)	(-4.81, 2.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-5.04, 5.13)
Week 24 (MMRM)		
n	78	68
LS mean (SE)	69.40 (2.24)	73.72 (2.39)
95% CI of LS mean	(64.97, 73.84)	(68.99, 78.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.32 (-2.17, 10.81)
Absolute Change at Week 24 (MMRM)		
n	78	67
LS mean (SE)	-2.01 (1.83)	-0.22 (1.97)
95% CI of LS mean	(-5.62, 1.59)	(-4.11, 3.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.79 (-3.52, 7.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	77	68
Mean (SD)	71.43 (21.13)	76.47 (17.44)
Absolute Change at Week 52		
n	77	66
Mean (SD)	0.87 (15.16)	2.36 (15.53)
Week 52 (MMRM)		
n	76	64
LS mean (SE)	72.71 (2.14)	76.96 (2.31)
95% CI of LS mean	(68.48, 76.94)	(72.40, 81.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.25 (-1.98, 10.48)
Absolute Change at Week 52 (MMRM)		
n	76	63
LS mean (SE)	1.32 (1.77)	3.02 (1.93)
95% CI of LS mean	(-2.18, 4.83)	(-0.81, 6.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.69 (-3.50, 6.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	78	68
LS mean (SE)	-0.61 (1.39)	0.57 (1.50)
95% CI of LS mean	(-3.36, 2.14)	(-2.40, 3.53)
P-value within Treatment	0.6619	0.7059
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.18 (-2.87, 5.23)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5665
Hedges' G (SE)		0.09 (0.17)
Hedges' 95% CI		(-0.23, 0.42)
Hedges' P-value		0.5661

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	83	84
Mean (SD)	72.82 (18.05)	74.74 (19.00)
Week 8 (MMRM)		
n	83	82
LS mean (SE)	71.10 (2.08)	73.26 (2.08)
95% CI of LS mean	(67.00, 75.20)	(69.15, 77.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.16 (-3.65, 7.97)
Absolute Change at Week 8 (MMRM)		
n	82	81
LS mean (SE)	-1.77 (1.49)	-1.79 (1.50)
95% CI of LS mean	(-4.71, 1.16)	(-4.75, 1.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.02 (-4.19, 4.15)
Week 16 (MMRM)		
n	83	83
LS mean (SE)	73.04 (2.20)	72.34 (2.20)
95% CI of LS mean	(68.70, 77.38)	(68.00, 76.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.70 (-6.84, 5.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	82	82
LS mean (SE)	-0.22 (1.58)	-2.63 (1.58)
95% CI of LS mean	(-3.33, 2.90)	(-5.74, 0.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.41 (-6.82, 1.99)
Week 24 (MMRM)		
n	83	82
LS mean (SE)	71.97 (2.17)	74.66 (2.18)
95% CI of LS mean	(67.68, 76.26)	(70.36, 78.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.69 (-3.39, 8.78)
Absolute Change at Week 24 (MMRM)		
n	82	81
LS mean (SE)	-1.03 (1.44)	-0.24 (1.45)
95% CI of LS mean	(-3.87, 1.81)	(-3.10, 2.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.78 (-3.25, 4.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	82	76
Mean (SD)	72.70 (19.99)	76.32 (19.23)
Absolute Change at Week 52		
n	81	75
Mean (SD)	0.34 (12.62)	1.78 (14.27)
Week 52 (MMRM)		
n	81	75
LS mean (SE)	73.58 (2.07)	76.54 (2.10)
95% CI of LS mean	(69.50, 77.66)	(72.40, 80.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.96 (-2.86, 8.78)
Absolute Change at Week 52 (MMRM)		
n	80	74
LS mean (SE)	0.66 (1.49)	1.53 (1.53)
95% CI of LS mean	(-2.27, 3.60)	(-1.49, 4.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.87 (-3.35, 5.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	82	82
LS mean (SE)	-0.19 (1.17)	-0.45 (1.18)
95% CI of LS mean	(-2.51, 2.12)	(-2.78, 1.88)
P-value within Treatment	0.8693	0.7052
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-3.54, 3.04)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8790
Hedges' G (SE)		-0.02 (0.16)
Hedges' 95% CI		(-0.33, 0.28)
Hedges' P-value		0.8789

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	106	103
Mean (SD)	69.81 (20.10)	73.25 (20.01)
Week 8 (MMRM)		
n	106	101
LS mean (SE)	69.85 (1.88)	72.74 (1.92)
95% CI of LS mean	(66.15, 73.56)	(68.95, 76.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.89 (-2.41, 8.19)
Absolute Change at Week 8 (MMRM)		
n	104	100
LS mean (SE)	-0.41 (1.43)	0.11 (1.45)
95% CI of LS mean	(-3.22, 2.40)	(-2.75, 2.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.52 (-3.50, 4.53)
Week 16 (MMRM)		
n	104	101
LS mean (SE)	70.08 (1.96)	73.25 (2.00)
95% CI of LS mean	(66.21, 73.94)	(69.30, 77.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.17 (-2.36, 8.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	102	100
LS mean (SE)	-0.33 (1.42)	0.64 (1.43)
95% CI of LS mean	(-3.12, 2.47)	(-2.19, 3.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-3.01, 4.94)
Week 24 (MMRM)		
n	104	101
LS mean (SE)	69.01 (2.07)	73.57 (2.11)
95% CI of LS mean	(64.93, 73.10)	(69.41, 77.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.56 (-1.27, 10.38)
Absolute Change at Week 24 (MMRM)		
n	102	100
LS mean (SE)	-1.44 (1.48)	0.51 (1.49)
95% CI of LS mean	(-4.35, 1.47)	(-2.44, 3.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.95 (-2.20, 6.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	102	103
Mean (SD)	72.66 (20.06)	74.00 (20.67)
Absolute Change at Week 52		
n	100	101
Mean (SD)	1.89 (13.12)	0.55 (15.59)
Week 52 (MMRM)		
n	101	100
LS mean (SE)	72.64 (2.00)	74.20 (2.03)
95% CI of LS mean	(68.69, 76.59)	(70.20, 78.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.56 (-4.06, 7.19)
Absolute Change at Week 52 (MMRM)		
n	99	99
LS mean (SE)	2.08 (1.45)	1.08 (1.46)
95% CI of LS mean	(-0.79, 4.95)	(-1.80, 3.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.00 (-5.07, 3.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	102	100
LS mean (SE)	0.10 (1.16)	0.74 (1.17)
95% CI of LS mean	(-2.19, 2.40)	(-1.57, 3.06)
P-value within Treatment	0.9287	0.5284
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.64 (-2.62, 3.90)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7000
Hedges' G (SE)		0.05 (0.14)
Hedges' 95% CI		(-0.22, 0.33)
Hedges' P-value		0.7000

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	111	99
Mean (SD)	79.65 (20.38)	77.73 (22.01)
Week 8 (MMRM)		
n	113	98
LS mean (SE)	76.86 (2.10)	78.55 (2.26)
95% CI of LS mean	(72.72, 81.01)	(74.10, 83.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.69 (-4.41, 7.78)
Absolute Change at Week 8 (MMRM)		
n	110	96
LS mean (SE)	-2.93 (1.66)	0.60 (1.78)
95% CI of LS mean	(-6.20, 0.35)	(-2.90, 4.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.53 (-1.28, 8.33)
Week 16 (MMRM)		
n	113	98
LS mean (SE)	76.26 (1.92)	80.70 (2.06)
95% CI of LS mean	(72.48, 80.04)	(76.64, 84.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.45 (-1.12, 10.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	110	96
LS mean (SE)	-3.48 (1.38)	2.69 (1.47)
95% CI of LS mean	(-6.19, -0.76)	(-0.22, 5.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.16 (2.18, 10.15)
Week 24 (MMRM)		
n	113	98
LS mean (SE)	78.79 (2.10)	78.26 (2.26)
95% CI of LS mean	(74.65, 82.94)	(73.81, 82.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.53 (-6.63, 5.57)
Absolute Change at Week 24 (MMRM)		
n	110	96
LS mean (SE)	-0.98 (1.45)	0.25 (1.56)
95% CI of LS mean	(-3.85, 1.89)	(-2.82, 3.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.23 (-2.98, 5.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	112	94
Mean (SD)	80.19 (20.14)	80.37 (20.64)
Absolute Change at Week 52		
n	109	92
Mean (SD)	-0.32 (13.42)	3.00 (12.70)
Week 52 (MMRM)		
n	112	93
LS mean (SE)	79.47 (1.91)	81.02 (2.06)
95% CI of LS mean	(75.71, 83.23)	(76.95, 85.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.55 (-4.00, 7.10)
Absolute Change at Week 52 (MMRM)		
n	109	91
LS mean (SE)	-0.29 (1.25)	3.05 (1.36)
95% CI of LS mean	(-2.75, 2.17)	(0.37, 5.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.34 (-0.30, 6.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	110	96
LS mean (SE)	-1.58 (1.07)	2.00 (1.15)
95% CI of LS mean	(-3.69, 0.52)	(-0.26, 4.25)
P-value within Treatment	0.1398	0.0832
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.58 (0.48, 6.68)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0239
Hedges' G (SE)		0.32 (0.14)
Hedges' 95% CI		(0.04, 0.59)
Hedges' P-value		0.0242

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	85	91
Mean (SD)	85.97 (15.36)	89.02 (15.26)
Week 8 (MMRM)		
n	84	90
LS mean (SE)	85.01 (1.96)	87.85 (1.88)
95% CI of LS mean	(81.15, 88.88)	(84.13, 91.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.84 (-2.53, 8.21)
Absolute Change at Week 8 (MMRM)		
n	83	90
LS mean (SE)	-1.01 (1.29)	-0.54 (1.24)
95% CI of LS mean	(-3.56, 1.55)	(-2.99, 1.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.46 (-3.08, 4.01)
Week 16 (MMRM)		
n	83	91
LS mean (SE)	86.03 (2.10)	86.77 (2.01)
95% CI of LS mean	(81.89, 90.17)	(82.81, 90.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.74 (-5.00, 6.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	82	90
LS mean (SE)	0.05 (1.68)	-1.88 (1.61)
95% CI of LS mean	(-3.28, 3.37)	(-5.06, 1.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.93 (-6.53, 2.68)
Week 24 (MMRM)		
n	83	90
LS mean (SE)	86.88 (1.76)	89.79 (1.69)
95% CI of LS mean	(83.42, 90.35)	(86.46, 93.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.91 (-1.90, 7.72)
Absolute Change at Week 24 (MMRM)		
n	82	89
LS mean (SE)	0.93 (1.24)	1.17 (1.19)
95% CI of LS mean	(-1.52, 3.38)	(-1.18, 3.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.23 (-3.16, 3.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	80	87
Mean (SD)	88.75 (14.96)	89.26 (16.16)
Absolute Change at Week 52		
n	79	86
Mean (SD)	3.12 (11.15)	0.92 (11.54)
Week 52 (MMRM)		
n	79	87
LS mean (SE)	88.68 (1.70)	89.65 (1.63)
95% CI of LS mean	(85.32, 92.04)	(86.43, 92.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-3.69, 5.63)
Absolute Change at Week 52 (MMRM)		
n	78	86
LS mean (SE)	2.86 (1.28)	1.10 (1.23)
95% CI of LS mean	(0.32, 5.40)	(-1.32, 3.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.76 (-5.27, 1.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	82	90
LS mean (SE)	1.28 (1.12)	0.13 (1.07)
95% CI of LS mean	(-0.93, 3.49)	(-1.99, 2.24)
P-value within Treatment	0.2545	0.9052
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.15 (-4.21, 1.91)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4586
Hedges' G (SE)		-0.11 (0.15)
Hedges' 95% CI		(-0.41, 0.19)
Hedges' P-value		0.4586

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	29	25
Mean (SD)	86.90 (15.96)	85.81 (14.90)
Week 8 (MMRM)		
n	29	24
LS mean (SE)	88.33 (2.62)	87.87 (2.88)
95% CI of LS mean	(83.05, 93.61)	(82.08, 93.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.46 (-8.35, 7.43)
Absolute Change at Week 8 (MMRM)		
n	28	24
LS mean (SE)	0.97 (2.22)	4.22 (2.43)
95% CI of LS mean	(-3.49, 5.43)	(-0.65, 9.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.26 (-3.38, 9.89)
Week 16 (MMRM)		
n	29	24
LS mean (SE)	88.74 (2.98)	87.21 (3.27)
95% CI of LS mean	(82.76, 94.71)	(80.65, 93.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.53 (-10.46, 7.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	28	23
LS mean (SE)	1.32 (1.91)	3.75 (2.10)
95% CI of LS mean	(-2.51, 5.15)	(-0.48, 7.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.43 (-3.31, 8.17)
Week 24 (MMRM)		
n	29	24
LS mean (SE)	87.20 (3.27)	84.58 (3.59)
95% CI of LS mean	(80.64, 93.76)	(77.37, 91.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.62 (-12.41, 7.17)
Absolute Change at Week 24 (MMRM)		
n	28	23
LS mean (SE)	-0.30 (2.33)	1.03 (2.57)
95% CI of LS mean	(-4.98, 4.38)	(-4.13, 6.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.33 (-5.66, 8.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	28	25
Mean (SD)	89.73 (16.26)	87.44 (16.58)
Absolute Change at Week 52		
n	27	24
Mean (SD)	1.73 (13.75)	3.55 (12.93)
Week 52 (MMRM)		
n	28	24
LS mean (SE)	88.88 (3.27)	87.53 (3.57)
95% CI of LS mean	(82.31, 95.46)	(80.35, 94.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.35 (-11.13, 8.43)
Absolute Change at Week 52 (MMRM)		
n	27	23
LS mean (SE)	1.42 (2.61)	4.40 (2.85)
95% CI of LS mean	(-3.82, 6.66)	(-1.33, 10.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.98 (-4.80, 10.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	28	23
LS mean (SE)	0.81 (1.95)	3.06 (2.15)
95% CI of LS mean	(-3.11, 4.74)	(-1.26, 7.38)
P-value within Treatment	0.6790	0.1610
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.25 (-3.63, 8.12)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4454
Hedges' G (SE)		0.21 (0.28)
Hedges' 95% CI		(-0.34, 0.77)
Hedges' P-value		0.4442

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	81.69 (18.93)	82.77 (20.41)
Week 8 (MMRM)		
n	168	164
LS mean (SE)	79.28 (1.63)	82.02 (1.64)
95% CI of LS mean	(76.08, 82.48)	(78.79, 85.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.74 (-1.81, 7.29)
Absolute Change at Week 8 (MMRM)		
n	165	162
LS mean (SE)	-2.57 (1.20)	-0.60 (1.21)
95% CI of LS mean	(-4.94, -0.20)	(-2.99, 1.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.97 (-1.40, 5.33)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	79.33 (1.57)	82.72 (1.58)
95% CI of LS mean	(76.25, 82.42)	(79.61, 85.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.38 (-1.00, 7.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	-2.49 (1.21)	-0.05 (1.22)
95% CI of LS mean	(-4.87, -0.10)	(-2.45, 2.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.43 (-0.95, 5.82)
Week 24 (MMRM)		
n	167	164
LS mean (SE)	81.78 (1.54)	83.33 (1.56)
95% CI of LS mean	(78.74, 84.81)	(80.27, 86.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.55 (-2.76, 5.86)
Absolute Change at Week 24 (MMRM)		
n	164	162
LS mean (SE)	-0.10 (1.07)	0.61 (1.08)
95% CI of LS mean	(-2.21, 2.01)	(-1.51, 2.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.71 (-2.28, 3.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	82.77 (18.78)	84.23 (19.30)
Absolute Change at Week 52		
n	162	156
Mean (SD)	0.97 (12.43)	1.76 (12.01)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	82.78 (1.42)	84.45 (1.44)
95% CI of LS mean	(79.98, 85.57)	(81.62, 87.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.68 (-2.30, 5.65)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	1.02 (0.96)	1.75 (0.98)
95% CI of LS mean	(-0.87, 2.91)	(-0.17, 3.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.73 (-1.97, 3.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	-0.52 (0.85)	0.77 (0.85)
95% CI of LS mean	(-2.19, 1.14)	(-0.90, 2.44)
P-value within Treatment	0.5381	0.3656
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.29 (-1.07, 3.65)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2824
Hedges' G (SE)		0.12 (0.11)
Hedges' 95% CI		(-0.10, 0.34)
Hedges' P-value		0.2826

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	80.92 (21.03)	73.40 (25.25)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	83.53 (4.34)	77.82 (4.74)
95% CI of LS mean	(74.67, 92.39)	(68.14, 87.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.72 (-19.04, 7.61)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	2.82 (3.28)	4.17 (3.58)
95% CI of LS mean	(-3.88, 9.52)	(-3.14, 11.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.35 (-8.66, 11.36)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	79.36 (4.09)	76.89 (4.48)
95% CI of LS mean	(71.00, 87.73)	(67.74, 86.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.48 (-15.10, 10.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-1.35 (2.78)	3.24 (3.04)
95% CI of LS mean	(-7.03, 4.33)	(-2.96, 9.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.59 (-3.94, 13.11)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	79.80 (3.96)	80.68 (4.33)
95% CI of LS mean	(71.71, 87.89)	(71.83, 89.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.88 (-11.34, 13.10)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	-0.91 (3.21)	7.03 (3.51)
95% CI of LS mean	(-7.46, 5.64)	(-0.12, 14.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.94 (-1.86, 17.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	85.19 (15.67)	75.89 (22.66)
Absolute Change at Week 52		
n	18	13
Mean (SD)	2.78 (13.63)	5.82 (11.88)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	84.37 (4.41)	77.68 (5.06)
95% CI of LS mean	(75.32, 93.41)	(67.33, 88.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.69 (-20.60, 7.22)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	3.05 (3.05)	5.47 (3.60)
95% CI of LS mean	(-3.19, 9.30)	(-1.90, 12.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.42 (-7.31, 12.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	0.26 (2.28)	5.25 (2.54)
95% CI of LS mean	(-4.40, 4.93)	(0.07, 10.43)
P-value within Treatment	0.9085	0.0473
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.98 (-2.12, 12.09)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1627
Hedges' G (SE)		0.48 (0.34)
Hedges' 95% CI		(-0.20, 1.17)
Hedges' P-value		0.1597

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	177	174
Mean (SD)	82.60 (18.40)	84.18 (19.11)
Week 8 (MMRM)		
n	178	172
LS mean (SE)	80.34 (1.53)	83.18 (1.56)
95% CI of LS mean	(77.33, 83.36)	(80.12, 86.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.84 (-1.46, 7.14)
Absolute Change at Week 8 (MMRM)		
n	174	170
LS mean (SE)	-2.61 (1.14)	-0.37 (1.15)
95% CI of LS mean	(-4.85, -0.36)	(-2.64, 1.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.24 (-0.95, 5.43)
Week 16 (MMRM)		
n	177	173
LS mean (SE)	80.89 (1.50)	83.87 (1.52)
95% CI of LS mean	(77.94, 83.84)	(80.88, 86.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.98 (-1.22, 7.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	173	170
LS mean (SE)	-1.99 (1.15)	0.16 (1.17)
95% CI of LS mean	(-4.27, 0.28)	(-2.13, 2.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.15 (-1.08, 5.38)
Week 24 (MMRM)		
n	177	172
LS mean (SE)	82.89 (1.50)	83.73 (1.52)
95% CI of LS mean	(79.95, 85.84)	(80.74, 86.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.84 (-3.36, 5.03)
Absolute Change at Week 24 (MMRM)		
n	173	169
LS mean (SE)	-0.05 (1.02)	0.05 (1.03)
95% CI of LS mean	(-2.05, 1.96)	(-1.97, 2.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-2.75, 2.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	174	169
Mean (SD)	83.66 (18.92)	85.57 (18.40)
Absolute Change at Week 52		
n	170	166
Mean (SD)	0.95 (12.52)	1.84 (12.02)
Week 52 (MMRM)		
n	173	167
LS mean (SE)	83.73 (1.37)	85.43 (1.39)
95% CI of LS mean	(81.04, 86.42)	(82.70, 88.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.70 (-2.13, 5.53)
Absolute Change at Week 52 (MMRM)		
n	169	164
LS mean (SE)	0.90 (0.94)	1.76 (0.96)
95% CI of LS mean	(-0.95, 2.76)	(-0.12, 3.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.85 (-1.79, 3.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	173	170
LS mean (SE)	-0.38 (0.82)	0.66 (0.83)
95% CI of LS mean	(-1.99, 1.24)	(-0.97, 2.29)
P-value within Treatment	0.6450	0.4284
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.04 (-1.26, 3.33)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3754
Hedges' G (SE)		0.10 (0.11)
Hedges' 95% CI		(-0.12, 0.31)
Hedges' P-value		0.3755

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	114	115
Mean (SD)	84.67 (18.30)	84.91 (18.63)
Week 8 (MMRM)		
n	116	116
LS mean (SE)	81.76 (1.83)	85.26 (1.84)
95% CI of LS mean	(78.15, 85.37)	(81.64, 88.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.49 (-1.64, 8.62)
Absolute Change at Week 8 (MMRM)		
n	112	115
LS mean (SE)	-3.20 (1.45)	0.65 (1.44)
95% CI of LS mean	(-6.07, -0.34)	(-2.18, 3.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.86 (-0.18, 7.89)
Week 16 (MMRM)		
n	115	115
LS mean (SE)	83.14 (1.71)	84.91 (1.71)
95% CI of LS mean	(79.77, 86.52)	(81.53, 88.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.76 (-3.03, 6.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	111	114
LS mean (SE)	-1.75 (1.26)	0.03 (1.24)
95% CI of LS mean	(-4.22, 0.73)	(-2.41, 2.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.78 (-1.71, 5.27)
Week 24 (MMRM)		
n	115	115
LS mean (SE)	84.61 (1.66)	85.89 (1.66)
95% CI of LS mean	(81.35, 87.88)	(82.61, 89.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.27 (-3.37, 5.91)
Absolute Change at Week 24 (MMRM)		
n	111	114
LS mean (SE)	-0.38 (1.20)	1.13 (1.19)
95% CI of LS mean	(-2.75, 1.99)	(-1.21, 3.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.51 (-1.83, 4.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	113	111
Mean (SD)	85.47 (17.98)	86.30 (18.57)
Absolute Change at Week 52		
n	109	110
Mean (SD)	0.51 (9.87)	1.80 (10.53)
Week 52 (MMRM)		
n	112	111
LS mean (SE)	85.17 (1.62)	86.88 (1.63)
95% CI of LS mean	(81.98, 88.37)	(83.68, 90.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.71 (-2.83, 6.25)
Absolute Change at Week 52 (MMRM)		
n	108	110
LS mean (SE)	0.39 (0.98)	1.98 (0.97)
95% CI of LS mean	(-1.54, 2.32)	(0.07, 3.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.59 (-1.14, 4.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	114
LS mean (SE)	-0.58 (0.90)	1.05 (0.89)
95% CI of LS mean	(-2.36, 1.20)	(-0.71, 2.80)
P-value within Treatment	0.5214	0.2418
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.63 (-0.88, 4.13)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2030
Hedges' G (SE)		0.17 (0.13)
Hedges' 95% CI		(-0.09, 0.43)
Hedges' P-value		0.2021

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	77
Mean (SD)	79.42 (18.63)	80.56 (21.24)
Week 8 (MMRM)		
n	81	72
LS mean (SE)	78.96 (2.32)	78.93 (2.44)
95% CI of LS mean	(74.38, 83.54)	(74.12, 83.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.02 (-6.68, 6.63)
Absolute Change at Week 8 (MMRM)		
n	81	71
LS mean (SE)	-0.72 (1.61)	-0.72 (1.72)
95% CI of LS mean	(-3.91, 2.46)	(-4.11, 2.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-4.65, 4.66)
Week 16 (MMRM)		
n	81	74
LS mean (SE)	77.22 (2.38)	80.90 (2.49)
95% CI of LS mean	(72.52, 81.93)	(75.98, 85.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.68 (-3.15, 10.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	81	72
LS mean (SE)	-2.42 (1.91)	1.27 (2.02)
95% CI of LS mean	(-6.19, 1.35)	(-2.73, 5.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.69 (-1.81, 9.19)
Week 24 (MMRM)		
n	81	73
LS mean (SE)	79.64 (2.42)	79.88 (2.54)
95% CI of LS mean	(74.85, 84.43)	(74.85, 84.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.24 (-6.72, 7.19)
Absolute Change at Week 24 (MMRM)		
n	81	71
LS mean (SE)	-0.02 (1.66)	0.14 (1.77)
95% CI of LS mean	(-3.30, 3.26)	(-3.36, 3.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-4.64, 4.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	80	73
Mean (SD)	81.39 (19.22)	82.17 (19.37)
Absolute Change at Week 52		
n	80	70
Mean (SD)	1.85 (15.58)	2.32 (14.33)
Week 52 (MMRM)		
n	79	69
LS mean (SE)	81.58 (2.14)	81.79 (2.26)
95% CI of LS mean	(77.34, 85.82)	(77.32, 86.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.21 (-5.96, 6.39)
Absolute Change at Week 52 (MMRM)		
n	79	67
LS mean (SE)	1.86 (1.69)	2.29 (1.82)
95% CI of LS mean	(-1.48, 5.20)	(-1.30, 5.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-4.48, 5.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	81	72
LS mean (SE)	-0.19 (1.39)	1.23 (1.48)
95% CI of LS mean	(-2.94, 2.55)	(-1.68, 4.15)
P-value within Treatment	0.8885	0.4051
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.43 (-2.58, 5.44)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4831
Hedges' G (SE)		0.11 (0.16)
Hedges' 95% CI		(-0.21, 0.43)
Hedges' P-value		0.4824

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	82.45 (17.92)	83.43 (20.91)
Week 8 (MMRM)		
n	88	83
LS mean (SE)	79.26 (2.33)	82.90 (2.39)
95% CI of LS mean	(74.66, 83.86)	(78.18, 87.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.65 (-2.95, 10.24)
Absolute Change at Week 8 (MMRM)		
n	86	82
LS mean (SE)	-3.51 (1.63)	0.22 (1.67)
95% CI of LS mean	(-6.73, -0.30)	(-3.07, 3.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.74 (-0.86, 8.34)
Week 16 (MMRM)		
n	89	85
LS mean (SE)	81.62 (2.18)	82.87 (2.24)
95% CI of LS mean	(77.31, 85.93)	(78.46, 87.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.25 (-4.92, 7.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	87	83
LS mean (SE)	-1.11 (1.62)	-0.07 (1.65)
95% CI of LS mean	(-4.30, 2.08)	(-3.34, 3.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.04 (-3.53, 5.61)
Week 24 (MMRM)		
n	89	84
LS mean (SE)	81.99 (2.34)	81.21 (2.40)
95% CI of LS mean	(77.37, 86.62)	(76.46, 85.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.79 (-7.42, 5.84)
Absolute Change at Week 24 (MMRM)		
n	87	82
LS mean (SE)	-0.73 (1.49)	-1.60 (1.54)
95% CI of LS mean	(-3.68, 2.22)	(-4.64, 1.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.87 (-5.11, 3.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	88	78
Mean (SD)	83.43 (18.79)	83.69 (21.21)
Absolute Change at Week 52		
n	86	76
Mean (SD)	0.76 (12.57)	1.24 (11.91)
Week 52 (MMRM)		
n	87	77
LS mean (SE)	83.51 (2.06)	84.06 (2.14)
95% CI of LS mean	(79.44, 87.58)	(79.84, 88.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.54 (-5.33, 6.41)
Absolute Change at Week 52 (MMRM)		
n	85	75
LS mean (SE)	0.88 (1.32)	1.36 (1.39)
95% CI of LS mean	(-1.72, 3.48)	(-1.38, 4.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.48 (-3.30, 4.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	87	83
LS mean (SE)	-0.32 (1.16)	-0.10 (1.19)
95% CI of LS mean	(-2.61, 1.97)	(-2.46, 2.25)
P-value within Treatment	0.7823	0.9307
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.22 (-3.07, 3.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8966
Hedges' G (SE)		0.02 (0.15)
Hedges' 95% CI		(-0.28, 0.32)
Hedges' P-value		0.8964

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	109	107
Mean (SD)	82.47 (19.17)	82.95 (18.92)
Week 8 (MMRM)		
n	109	105
LS mean (SE)	81.75 (1.79)	82.70 (1.82)
95% CI of LS mean	(78.22, 85.27)	(79.11, 86.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.95 (-4.08, 5.99)
Absolute Change at Week 8 (MMRM)		
n	107	104
LS mean (SE)	-0.94 (1.43)	-0.06 (1.45)
95% CI of LS mean	(-3.77, 1.88)	(-2.93, 2.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.88 (-3.14, 4.90)
Week 16 (MMRM)		
n	107	104
LS mean (SE)	79.93 (1.85)	83.67 (1.88)
95% CI of LS mean	(76.28, 83.58)	(79.96, 87.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.74 (-1.47, 8.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	105	103
LS mean (SE)	-2.66 (1.46)	0.86 (1.48)
95% CI of LS mean	(-5.54, 0.22)	(-2.05, 3.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.52 (-0.57, 7.62)
Week 24 (MMRM)		
n	107	104
LS mean (SE)	83.01 (1.65)	85.36 (1.67)
95% CI of LS mean	(79.77, 86.26)	(82.06, 88.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.34 (-2.29, 6.97)
Absolute Change at Week 24 (MMRM)		
n	105	103
LS mean (SE)	0.32 (1.26)	2.52 (1.27)
95% CI of LS mean	(-2.16, 2.80)	(0.01, 5.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.20 (-1.33, 5.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	105	106
Mean (SD)	84.07 (18.45)	85.38 (17.16)
Absolute Change at Week 52		
n	103	104
Mean (SD)	1.34 (12.66)	2.55 (12.29)
Week 52 (MMRM)		
n	104	103
LS mean (SE)	83.83 (1.65)	85.49 (1.67)
95% CI of LS mean	(80.57, 87.08)	(82.19, 88.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.67 (-2.97, 6.31)
Absolute Change at Week 52 (MMRM)		
n	102	102
LS mean (SE)	1.23 (1.23)	2.66 (1.23)
95% CI of LS mean	(-1.19, 3.65)	(0.23, 5.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.43 (-2.00, 4.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	105	103
LS mean (SE)	-0.37 (1.04)	2.01 (1.05)
95% CI of LS mean	(-2.42, 1.68)	(-0.05, 4.08)
P-value within Treatment	0.7228	0.0563
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-0.53, 5.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1082
Hedges' G (SE)		0.22 (0.14)
Hedges' 95% CI		(-0.05, 0.50)
Hedges' P-value		0.1092

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	108	98
Mean (SD)	85.49 (19.81)	84.27 (18.34)
Week 8 (MMRM)		
n	109	98
LS mean (SE)	84.78 (1.59)	86.36 (1.68)
95% CI of LS mean	(81.65, 87.92)	(83.05, 89.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.57 (-3.00, 6.14)
Absolute Change at Week 8 (MMRM)		
n	107	95
LS mean (SE)	-0.80 (1.31)	2.13 (1.39)
95% CI of LS mean	(-3.38, 1.79)	(-0.61, 4.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.93 (-0.85, 6.71)
Week 16 (MMRM)		
n	109	98
LS mean (SE)	84.25 (1.61)	88.25 (1.70)
95% CI of LS mean	(81.07, 87.42)	(84.91, 91.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.01 (-0.61, 8.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	107	95
LS mean (SE)	-1.22 (1.49)	4.89 (1.59)
95% CI of LS mean	(-4.17, 1.72)	(1.77, 8.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.12 (1.81, 10.42)
Week 24 (MMRM)		
n	109	97
LS mean (SE)	86.14 (1.61)	87.06 (1.70)
95% CI of LS mean	(82.97, 89.30)	(83.72, 90.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.92 (-3.69, 5.54)
Absolute Change at Week 24 (MMRM)		
n	107	94
LS mean (SE)	0.35 (1.44)	3.22 (1.53)
95% CI of LS mean	(-2.48, 3.18)	(0.21, 6.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.87 (-1.27, 7.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	108	94
Mean (SD)	87.58 (15.97)	88.12 (14.89)
Absolute Change at Week 52		
n	106	91
Mean (SD)	1.34 (12.76)	4.49 (14.61)
Week 52 (MMRM)		
n	108	93
LS mean (SE)	87.20 (1.47)	88.33 (1.57)
95% CI of LS mean	(84.29, 90.11)	(85.24, 91.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.13 (-3.12, 5.39)
Absolute Change at Week 52 (MMRM)		
n	106	90
LS mean (SE)	1.47 (1.33)	4.32 (1.43)
95% CI of LS mean	(-1.15, 4.10)	(1.50, 7.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.85 (-1.01, 6.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	107	95
LS mean (SE)	0.20 (1.23)	4.15 (1.30)
95% CI of LS mean	(-2.22, 2.62)	(1.58, 6.72)
P-value within Treatment	0.8707	0.0017
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.95 (0.41, 7.48)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0290
Hedges' G (SE)		0.31 (0.14)
Hedges' 95% CI		(0.03, 0.59)
Hedges' P-value		0.0294

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	80	86
Mean (SD)	90.52 (11.62)	90.70 (11.53)
Week 8 (MMRM)		
n	79	85
LS mean (SE)	89.96 (1.44)	89.53 (1.39)
95% CI of LS mean	(87.12, 92.80)	(86.80, 92.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.43 (-4.37, 3.52)
Absolute Change at Week 8 (MMRM)		
n	78	85
LS mean (SE)	-0.63 (1.33)	-1.07 (1.27)
95% CI of LS mean	(-3.25, 1.99)	(-3.58, 1.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.45 (-4.08, 3.18)
Week 16 (MMRM)		
n	78	86
LS mean (SE)	87.98 (1.64)	89.69 (1.57)
95% CI of LS mean	(84.75, 91.22)	(86.60, 92.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.71 (-2.77, 6.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	77	86
LS mean (SE)	-2.43 (1.43)	-0.97 (1.36)
95% CI of LS mean	(-5.26, 0.40)	(-3.65, 1.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.46 (-2.44, 5.37)
Week 24 (MMRM)		
n	78	85
LS mean (SE)	87.66 (1.49)	89.72 (1.43)
95% CI of LS mean	(84.72, 90.60)	(86.90, 92.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.05 (-2.02, 6.13)
Absolute Change at Week 24 (MMRM)		
n	77	85
LS mean (SE)	-2.76 (1.39)	-0.92 (1.32)
95% CI of LS mean	(-5.51, -0.02)	(-3.53, 1.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.85 (-1.94, 5.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	74	82
Mean (SD)	90.43 (12.77)	89.13 (14.85)
Absolute Change at Week 52		
n	73	82
Mean (SD)	0.57 (11.73)	-1.12 (14.33)
Week 52 (MMRM)		
n	73	82
LS mean (SE)	90.49 (1.59)	89.42 (1.52)
95% CI of LS mean	(87.34, 93.64)	(86.43, 92.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.06 (-5.41, 3.28)
Absolute Change at Week 52 (MMRM)		
n	72	82
LS mean (SE)	0.22 (1.53)	-1.15 (1.45)
95% CI of LS mean	(-2.81, 3.25)	(-4.01, 1.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.37 (-5.53, 2.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	77	86
LS mean (SE)	-1.66 (1.16)	-1.01 (1.11)
95% CI of LS mean	(-3.96, 0.64)	(-3.20, 1.17)
P-value within Treatment	0.1558	0.3619
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.65 (-2.53, 3.82)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6875
Hedges' G (SE)		0.06 (0.16)
Hedges' 95% CI		(-0.25, 0.37)
Hedges' P-value		0.6874

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	21	20
Mean (SD)	86.90 (12.79)	88.75 (10.57)
Week 8 (MMRM)		
n	21	19
LS mean (SE)	87.08 (2.77)	89.28 (2.91)
95% CI of LS mean	(81.47, 92.70)	(83.37, 95.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.19 (-5.98, 10.36)
Absolute Change at Week 8 (MMRM)		
n	21	19
LS mean (SE)	0.18 (3.53)	0.68 (3.71)
95% CI of LS mean	(-6.98, 7.34)	(-6.85, 8.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-9.92, 10.91)
Week 16 (MMRM)		
n	20	19
LS mean (SE)	86.35 (2.84)	89.72 (2.93)
95% CI of LS mean	(80.59, 92.11)	(83.77, 95.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.37 (-4.94, 11.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	20	19
LS mean (SE)	-0.48 (3.27)	1.12 (3.39)
95% CI of LS mean	(-7.11, 6.14)	(-5.75, 7.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.60 (-7.97, 11.17)
Week 24 (MMRM)		
n	20	19
LS mean (SE)	83.81 (3.16)	87.08 (3.27)
95% CI of LS mean	(77.41, 90.21)	(80.46, 93.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.28 (-5.96, 12.51)
Absolute Change at Week 24 (MMRM)		
n	20	19
LS mean (SE)	-3.05 (3.70)	-1.52 (3.85)
95% CI of LS mean	(-10.55, 4.44)	(-9.31, 6.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.54 (-9.30, 12.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	18	20
Mean (SD)	85.19 (17.04)	90.42 (13.04)
Absolute Change at Week 52		
n	18	20
Mean (SD)	-1.85 (16.06)	1.67 (11.97)
Week 52 (MMRM)		
n	18	19
LS mean (SE)	84.85 (3.51)	89.72 (3.49)
95% CI of LS mean	(77.75, 91.95)	(82.64, 96.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.87 (-5.17, 14.91)
Absolute Change at Week 52 (MMRM)		
n	18	19
LS mean (SE)	-1.84 (3.32)	1.12 (3.31)
95% CI of LS mean	(-8.55, 4.88)	(-5.61, 7.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.95 (-6.58, 12.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	20	19
LS mean (SE)	-1.79 (2.79)	0.24 (2.90)
95% CI of LS mean	(-7.45, 3.86)	(-5.64, 6.11)
P-value within Treatment	0.5249	0.9349
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.03 (-6.16, 10.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6184
Hedges' G (SE)		0.16 (0.31)
Hedges' 95% CI		(-0.48, 0.80)
Hedges' P-value		0.6173

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	166
Mean (SD)	87.75 (17.40)	87.20 (16.30)
Week 8 (MMRM)		
n	167	164
LS mean (SE)	87.10 (1.18)	87.54 (1.19)
95% CI of LS mean	(84.78, 89.41)	(85.20, 89.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.44 (-2.85, 3.73)
Absolute Change at Week 8 (MMRM)		
n	164	161
LS mean (SE)	-0.71 (0.97)	0.47 (0.98)
95% CI of LS mean	(-2.62, 1.21)	(-1.46, 2.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-1.55, 3.89)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	85.89 (1.25)	88.69 (1.25)
95% CI of LS mean	(83.44, 88.34)	(86.22, 91.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.80 (-0.68, 6.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	162
LS mean (SE)	-1.74 (1.13)	2.08 (1.14)
95% CI of LS mean	(-3.96, 0.48)	(-0.15, 4.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.82 (0.67, 6.97)
Week 24 (MMRM)		
n	167	163
LS mean (SE)	87.29 (1.19)	88.30 (1.20)
95% CI of LS mean	(84.95, 89.62)	(85.94, 90.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.01 (-2.31, 4.34)
Absolute Change at Week 24 (MMRM)		
n	164	160
LS mean (SE)	-0.57 (1.05)	1.45 (1.06)
95% CI of LS mean	(-2.63, 1.49)	(-0.63, 3.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.02 (-0.91, 4.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	89.19 (14.50)	88.52 (14.99)
Absolute Change at Week 52		
n	162	155
Mean (SD)	1.39 (11.83)	1.83 (14.99)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	89.16 (1.14)	88.57 (1.16)
95% CI of LS mean	(86.92, 91.40)	(86.29, 90.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.60 (-3.79, 2.59)
Absolute Change at Week 52 (MMRM)		
n	160	153
LS mean (SE)	1.43 (1.06)	1.60 (1.08)
95% CI of LS mean	(-0.67, 3.52)	(-0.52, 3.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-2.81, 3.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	162
LS mean (SE)	-0.29 (0.91)	1.71 (0.92)
95% CI of LS mean	(-2.09, 1.51)	(-0.11, 3.53)
P-value within Treatment	0.7479	0.0648
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.00 (-0.55, 4.56)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1241
Hedges' G (SE)		0.17 (0.11)
Hedges' 95% CI		(-0.05, 0.39)
Hedges' P-value		0.1246

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	88.16 (15.29)	82.81 (17.34)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	88.26 (3.32)	88.42 (3.62)
95% CI of LS mean	(81.50, 95.02)	(81.04, 95.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-9.93, 10.25)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	-1.72 (2.34)	7.78 (2.56)
95% CI of LS mean	(-6.50, 3.05)	(2.56, 12.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.50 (2.35, 16.65)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	80.37 (3.72)	85.82 (4.06)
95% CI of LS mean	(72.79, 87.94)	(77.55, 94.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.45 (-5.85, 16.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-9.62 (3.10)	5.17 (3.39)
95% CI of LS mean	(-15.94, -3.30)	(-1.72, 12.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.79 (5.38, 24.20)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	87.38 (2.95)	84.25 (3.22)
95% CI of LS mean	(81.37, 93.39)	(77.69, 90.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.13 (-12.13, 5.87)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	-2.60 (3.77)	3.61 (4.11)
95% CI of LS mean	(-10.29, 5.09)	(-4.77, 11.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.21 (-5.21, 17.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	90.74 (10.26)	87.50 (9.10)
Absolute Change at Week 52		
n	18	13
Mean (SD)	1.39 (8.69)	6.41 (13.24)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	91.06 (2.21)	86.25 (2.53)
95% CI of LS mean	(86.54, 95.59)	(81.09, 91.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.81 (-11.78, 2.16)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	0.57 (2.52)	6.61 (2.87)
95% CI of LS mean	(-4.59, 5.73)	(0.74, 12.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.04 (-1.83, 13.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	-3.88 (2.59)	5.13 (2.84)
95% CI of LS mean	(-9.17, 1.41)	(-0.67, 10.93)
P-value within Treatment	0.1444	0.0810
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.01 (1.10, 16.92)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0269
Hedges' G (SE)		0.78 (0.34)
Hedges' 95% CI		(0.08, 1.48)
Hedges' P-value		0.0307

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	169	168
Mean (SD)	87.52 (17.16)	87.75 (15.66)
Week 8 (MMRM)		
n	169	167
LS mean (SE)	86.99 (1.16)	87.62 (1.16)
95% CI of LS mean	(84.72, 89.27)	(85.33, 89.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.62 (-2.60, 3.85)
Absolute Change at Week 8 (MMRM)		
n	166	164
LS mean (SE)	-0.65 (1.01)	-0.06 (1.02)
95% CI of LS mean	(-2.64, 1.33)	(-2.06, 1.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.60 (-2.23, 3.42)
Week 16 (MMRM)		
n	168	168
LS mean (SE)	86.60 (1.22)	89.05 (1.22)
95% CI of LS mean	(84.20, 88.99)	(86.65, 91.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.45 (-0.94, 5.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	165	165
LS mean (SE)	-0.85 (1.12)	1.85 (1.12)
95% CI of LS mean	(-3.04, 1.35)	(-0.36, 4.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.69 (-0.42, 5.81)
Week 24 (MMRM)		
n	168	166
LS mean (SE)	86.89 (1.19)	88.52 (1.20)
95% CI of LS mean	(84.55, 89.23)	(86.17, 90.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.63 (-1.69, 4.95)
Absolute Change at Week 24 (MMRM)		
n	165	163
LS mean (SE)	-0.79 (1.06)	1.07 (1.06)
95% CI of LS mean	(-2.87, 1.29)	(-1.02, 3.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.87 (-1.08, 4.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	164	164
Mean (SD)	88.52 (15.20)	88.87 (15.20)
Absolute Change at Week 52		
n	161	161
Mean (SD)	1.04 (12.70)	1.45 (14.78)
Week 52 (MMRM)		
n	163	162
LS mean (SE)	88.50 (1.17)	88.89 (1.18)
95% CI of LS mean	(86.19, 90.81)	(86.57, 91.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.39 (-2.89, 3.66)
Absolute Change at Week 52 (MMRM)		
n	160	159
LS mean (SE)	0.94 (1.08)	1.31 (1.09)
95% CI of LS mean	(-1.19, 3.08)	(-0.84, 3.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-2.66, 3.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	165	165
LS mean (SE)	-0.23 (0.92)	1.41 (0.92)
95% CI of LS mean	(-2.04, 1.58)	(-0.41, 3.23)
P-value within Treatment	0.8011	0.1279
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.64 (-0.93, 4.21)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2094
Hedges' G (SE)		0.14 (0.11)
Hedges' 95% CI		(-0.08, 0.35)
Hedges' P-value		0.2095

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	109	113
Mean (SD)	88.07 (17.36)	89.16 (13.81)
Week 8 (MMRM)		
n	109	115
LS mean (SE)	88.80 (1.39)	88.53 (1.36)
95% CI of LS mean	(86.07, 91.54)	(85.85, 91.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.28 (-4.11, 3.55)
Absolute Change at Week 8 (MMRM)		
n	106	113
LS mean (SE)	0.64 (1.23)	-0.65 (1.19)
95% CI of LS mean	(-1.78, 3.07)	(-3.00, 1.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.29 (-4.67, 2.09)
Week 16 (MMRM)		
n	109	115
LS mean (SE)	86.12 (1.53)	89.61 (1.49)
95% CI of LS mean	(83.11, 89.13)	(86.67, 92.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.49 (-0.72, 7.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	106	113
LS mean (SE)	-1.84 (1.24)	0.61 (1.21)
95% CI of LS mean	(-4.29, 0.61)	(-1.77, 2.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.45 (-0.97, 5.87)
Week 24 (MMRM)		
n	109	114
LS mean (SE)	88.65 (1.37)	89.53 (1.34)
95% CI of LS mean	(85.94, 91.36)	(86.88, 92.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.88 (-2.92, 4.67)
Absolute Change at Week 24 (MMRM)		
n	106	112
LS mean (SE)	0.37 (1.24)	0.61 (1.21)
95% CI of LS mean	(-2.08, 2.82)	(-1.77, 3.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.24 (-3.18, 3.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	107	111
Mean (SD)	89.64 (14.29)	88.96 (15.50)
Absolute Change at Week 52		
n	104	109
Mean (SD)	1.36 (10.71)	0.08 (12.24)
Week 52 (MMRM)		
n	106	111
LS mean (SE)	89.50 (1.42)	89.24 (1.39)
95% CI of LS mean	(86.70, 92.30)	(86.50, 91.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-4.19, 3.66)
Absolute Change at Week 52 (MMRM)		
n	103	109
LS mean (SE)	1.36 (1.13)	0.09 (1.10)
95% CI of LS mean	(-0.87, 3.59)	(-2.08, 2.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.27 (-4.39, 1.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	106	113
LS mean (SE)	-0.04 (1.01)	0.44 (0.98)
95% CI of LS mean	(-2.02, 1.95)	(-1.49, 2.37)
P-value within Treatment	0.9709	0.6552
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.47 (-2.30, 3.25)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7364
Hedges' G (SE)		0.05 (0.13)
Hedges' 95% CI		(-0.22, 0.31)
Hedges' P-value		0.7359

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	80	73
Mean (SD)	87.08 (16.40)	84.59 (18.14)
Week 8 (MMRM)		
n	79	68
LS mean (SE)	84.60 (1.76)	86.49 (1.88)
95% CI of LS mean	(81.13, 88.07)	(82.77, 90.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.89 (-3.20, 6.98)
Absolute Change at Week 8 (MMRM)		
n	79	67
LS mean (SE)	-2.43 (1.45)	2.53 (1.57)
95% CI of LS mean	(-5.30, 0.44)	(-0.56, 5.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.96 (0.74, 9.19)
Week 16 (MMRM)		
n	78	69
LS mean (SE)	85.59 (1.78)	87.49 (1.89)
95% CI of LS mean	(82.08, 89.11)	(83.75, 91.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.90 (-3.24, 7.04)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	78	68
LS mean (SE)	-1.41 (1.87)	4.36 (2.00)
95% CI of LS mean	(-5.10, 2.28)	(0.41, 8.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.77 (0.36, 11.18)
Week 24 (MMRM)		
n	78	68
LS mean (SE)	84.42 (1.85)	85.98 (1.97)
95% CI of LS mean	(80.77, 88.07)	(82.09, 89.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.56 (-3.78, 6.91)
Absolute Change at Week 24 (MMRM)		
n	78	67
LS mean (SE)	-2.59 (1.71)	2.07 (1.84)
95% CI of LS mean	(-5.97, 0.79)	(-1.56, 5.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.66 (-0.30, 9.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	76	68
Mean (SD)	87.61 (15.43)	88.36 (13.59)
Absolute Change at Week 52		
n	76	66
Mean (SD)	0.66 (14.26)	4.67 (17.67)
Week 52 (MMRM)		
n	75	64
LS mean (SE)	87.54 (1.68)	88.00 (1.80)
95% CI of LS mean	(84.23, 90.86)	(84.43, 91.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-4.42, 5.33)
Absolute Change at Week 52 (MMRM)		
n	75	63
LS mean (SE)	0.57 (1.83)	4.12 (1.98)
95% CI of LS mean	(-3.06, 4.19)	(0.20, 8.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.55 (-1.79, 8.89)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	78	68
LS mean (SE)	-1.14 (1.53)	3.52 (1.65)
95% CI of LS mean	(-4.18, 1.89)	(0.26, 6.77)
P-value within Treatment	0.4570	0.0344
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.66 (0.21, 9.11)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0403
Hedges' G (SE)		0.34 (0.17)
Hedges' 95% CI		(0.01, 0.67)
Hedges' P-value		0.0416

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	83	84
Mean (SD)	92.07 (12.13)	88.19 (14.18)
Week 8 (MMRM)		
n	83	82
LS mean (SE)	88.59 (1.65)	87.05 (1.65)
95% CI of LS mean	(85.34, 91.84)	(83.79, 90.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.54 (-6.15, 3.07)
Absolute Change at Week 8 (MMRM)		
n	82	81
LS mean (SE)	-3.34 (1.20)	-1.36 (1.21)
95% CI of LS mean	(-5.72, -0.96)	(-3.76, 1.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.98 (-1.40, 5.35)
Week 16 (MMRM)		
n	83	83
LS mean (SE)	89.49 (1.60)	88.72 (1.60)
95% CI of LS mean	(86.33, 92.66)	(85.56, 91.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.77 (-5.25, 3.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	82	82
LS mean (SE)	-2.32 (1.28)	0.59 (1.28)
95% CI of LS mean	(-4.84, 0.20)	(-1.92, 3.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.92 (-0.65, 6.48)
Week 24 (MMRM)		
n	83	81
LS mean (SE)	87.89 (1.79)	87.35 (1.80)
95% CI of LS mean	(84.35, 91.42)	(83.79, 90.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.54 (-5.56, 4.48)
Absolute Change at Week 24 (MMRM)		
n	82	80
LS mean (SE)	-3.95 (1.31)	-0.65 (1.33)
95% CI of LS mean	(-6.54, -1.36)	(-3.27, 1.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.30 (-0.39, 6.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	82	76
Mean (SD)	91.77 (12.11)	87.83 (15.12)
Absolute Change at Week 52		
n	81	75
Mean (SD)	-0.10 (9.46)	0.33 (10.29)
Week 52 (MMRM)		
n	81	75
LS mean (SE)	91.74 (1.48)	88.18 (1.51)
95% CI of LS mean	(88.81, 94.67)	(85.20, 91.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.56 (-7.74, 0.62)
Absolute Change at Week 52 (MMRM)		
n	80	74
LS mean (SE)	-0.04 (1.11)	0.16 (1.14)
95% CI of LS mean	(-2.22, 2.15)	(-2.09, 2.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.20 (-2.94, 3.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	82	82
LS mean (SE)	-2.10 (0.95)	0.03 (0.95)
95% CI of LS mean	(-3.97, -0.23)	(-1.85, 1.92)
P-value within Treatment	0.0279	0.9709
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.14 (-0.52, 4.80)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1141
Hedges' G (SE)		0.25 (0.16)
Hedges' 95% CI		(-0.06, 0.56)
Hedges' P-value		0.1151

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	106	102
Mean (SD)	84.20 (19.24)	86.68 (17.00)
Week 8 (MMRM)		
n	105	101
LS mean (SE)	85.86 (1.44)	88.45 (1.48)
95% CI of LS mean	(83.02, 88.71)	(85.54, 91.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.59 (-1.49, 6.66)
Absolute Change at Week 8 (MMRM)		
n	103	99
LS mean (SE)	1.53 (1.37)	2.13 (1.40)
95% CI of LS mean	(-1.17, 4.24)	(-0.64, 4.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.60 (-3.28, 4.47)
Week 16 (MMRM)		
n	104	101
LS mean (SE)	83.00 (1.63)	88.98 (1.66)
95% CI of LS mean	(79.79, 86.21)	(85.71, 92.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.98 (1.40, 10.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	102	99
LS mean (SE)	-1.10 (1.63)	3.20 (1.66)
95% CI of LS mean	(-4.32, 2.11)	(-0.07, 6.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.31 (-0.28, 8.89)
Week 24 (MMRM)		
n	104	101
LS mean (SE)	86.04 (1.40)	88.99 (1.43)
95% CI of LS mean	(83.28, 88.80)	(86.17, 91.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.95 (-0.99, 6.89)
Absolute Change at Week 24 (MMRM)		
n	102	99
LS mean (SE)	1.61 (1.47)	2.69 (1.50)
95% CI of LS mean	(-1.29, 4.50)	(-0.26, 5.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.09 (-3.05, 5.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	101	103
Mean (SD)	86.39 (16.28)	89.40 (14.54)
Absolute Change at Week 52		
n	99	100
Mean (SD)	2.02 (14.19)	2.92 (17.18)
Week 52 (MMRM)		
n	100	100
LS mean (SE)	86.13 (1.53)	89.30 (1.54)
95% CI of LS mean	(83.12, 89.14)	(86.26, 92.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.17 (-1.11, 7.45)
Absolute Change at Week 52 (MMRM)		
n	98	98
LS mean (SE)	1.78 (1.58)	2.95 (1.60)
95% CI of LS mean	(-1.33, 4.89)	(-0.20, 6.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-3.26, 5.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	102	99
LS mean (SE)	0.76 (1.36)	2.95 (1.38)
95% CI of LS mean	(-1.92, 3.44)	(0.22, 5.68)
P-value within Treatment	0.5761	0.0343
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.19 (-1.64, 6.01)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2604
Hedges' G (SE)		0.16 (0.14)
Hedges' 95% CI		(-0.12, 0.44)
Hedges' P-value		0.2610

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	111	99
Mean (SD)	71.53 (17.81)	72.28 (18.71)
Week 8 (MMRM)		
n	113	98
LS mean (SE)	74.46 (1.62)	73.79 (1.73)
95% CI of LS mean	(71.27, 77.64)	(70.37, 77.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.67 (-5.35, 4.02)
Absolute Change at Week 8 (MMRM)		
n	110	96
LS mean (SE)	2.82 (1.20)	1.54 (1.28)
95% CI of LS mean	(0.47, 5.18)	(-0.98, 4.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.28 (-4.75, 2.18)
Week 16 (MMRM)		
n	113	98
LS mean (SE)	73.21 (1.82)	71.99 (1.95)
95% CI of LS mean	(69.63, 76.80)	(68.13, 75.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.23 (-6.50, 4.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	110	96
LS mean (SE)	1.45 (1.41)	-0.12 (1.51)
95% CI of LS mean	(-1.34, 4.23)	(-3.10, 2.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.56 (-5.65, 2.52)
Week 24 (MMRM)		
n	113	98
LS mean (SE)	75.35 (1.69)	73.52 (1.82)
95% CI of LS mean	(72.01, 78.69)	(69.93, 77.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.83 (-6.74, 3.07)
Absolute Change at Week 24 (MMRM)		
n	110	96
LS mean (SE)	3.64 (1.23)	1.39 (1.32)
95% CI of LS mean	(1.22, 6.07)	(-1.21, 3.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.26 (-5.82, 1.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	112	94
Mean (SD)	76.45 (16.36)	74.88 (18.70)
Absolute Change at Week 52		
n	109	92
Mean (SD)	4.27 (13.36)	2.84 (15.02)
Week 52 (MMRM)		
n	112	93
LS mean (SE)	76.13 (1.65)	75.25 (1.79)
95% CI of LS mean	(72.87, 79.39)	(71.72, 78.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.89 (-5.70, 3.93)
Absolute Change at Week 52 (MMRM)		
n	109	91
LS mean (SE)	4.35 (1.35)	2.79 (1.47)
95% CI of LS mean	(1.68, 7.02)	(-0.10, 5.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.56 (-5.51, 2.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	110	96
LS mean (SE)	3.15 (1.16)	1.35 (1.24)
95% CI of LS mean	(0.86, 5.44)	(-1.10, 3.81)
P-value within Treatment	0.0072	0.2780
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.79 (-5.16, 1.57)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2943
Hedges' G (SE)		-0.15 (0.14)
Hedges' 95% CI		(-0.42, 0.13)
Hedges' P-value		0.2934

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	85	91
Mean (SD)	77.56 (15.64)	77.68 (17.57)
Week 8 (MMRM)		
n	84	90
LS mean (SE)	76.71 (1.86)	78.03 (1.80)
95% CI of LS mean	(73.04, 80.39)	(74.49, 81.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.32 (-3.79, 6.43)
Absolute Change at Week 8 (MMRM)		
n	83	90
LS mean (SE)	-1.13 (1.62)	0.61 (1.56)
95% CI of LS mean	(-4.34, 2.07)	(-2.47, 3.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.74 (-2.71, 6.19)
Week 16 (MMRM)		
n	83	91
LS mean (SE)	76.63 (1.88)	77.30 (1.80)
95% CI of LS mean	(72.91, 80.34)	(73.74, 80.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.68 (-4.47, 5.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	82	90
LS mean (SE)	-1.44 (1.57)	-0.22 (1.51)
95% CI of LS mean	(-4.55, 1.67)	(-3.19, 2.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.23 (-3.08, 5.53)
Week 24 (MMRM)		
n	83	90
LS mean (SE)	77.73 (1.77)	80.37 (1.69)
95% CI of LS mean	(74.25, 81.22)	(77.02, 83.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.64 (-2.20, 7.47)
Absolute Change at Week 24 (MMRM)		
n	82	89
LS mean (SE)	-0.30 (1.47)	2.86 (1.41)
95% CI of LS mean	(-3.20, 2.61)	(0.07, 5.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.15 (-0.88, 7.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	80	87
Mean (SD)	79.19 (15.72)	79.97 (15.85)
Absolute Change at Week 52		
n	79	86
Mean (SD)	1.66 (13.56)	2.76 (13.43)
Week 52 (MMRM)		
n	79	87
LS mean (SE)	79.61 (1.72)	80.25 (1.65)
95% CI of LS mean	(76.22, 83.00)	(77.00, 83.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.64 (-4.06, 5.34)
Absolute Change at Week 52 (MMRM)		
n	78	86
LS mean (SE)	1.66 (1.50)	2.91 (1.43)
95% CI of LS mean	(-1.29, 4.61)	(0.09, 5.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.24 (-2.84, 5.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	82	90
LS mean (SE)	-0.03 (1.24)	1.85 (1.19)
95% CI of LS mean	(-2.47, 2.42)	(-0.49, 4.19)
P-value within Treatment	0.9836	0.1211
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.87 (-1.52, 5.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2767
Hedges' G (SE)		0.17 (0.15)
Hedges' 95% CI		(-0.13, 0.47)
Hedges' P-value		0.2770

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	29	25
Mean (SD)	72.50 (15.29)	77.65 (13.56)
Week 8 (MMRM)		
n	29	24
LS mean (SE)	73.35 (2.83)	76.91 (3.10)
95% CI of LS mean	(67.67, 79.02)	(70.68, 83.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.56 (-4.90, 12.02)
Absolute Change at Week 8 (MMRM)		
n	28	24
LS mean (SE)	0.53 (2.63)	0.69 (2.87)
95% CI of LS mean	(-4.76, 5.82)	(-5.08, 6.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-7.70, 8.03)
Week 16 (MMRM)		
n	29	24
LS mean (SE)	74.37 (2.57)	75.54 (2.82)
95% CI of LS mean	(69.21, 79.53)	(69.87, 81.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-6.54, 8.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	28	23
LS mean (SE)	1.13 (2.50)	-1.13 (2.76)
95% CI of LS mean	(-3.91, 6.16)	(-6.68, 4.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.25 (-9.79, 5.28)
Week 24 (MMRM)		
n	29	24
LS mean (SE)	75.29 (2.36)	77.69 (2.59)
95% CI of LS mean	(70.55, 80.03)	(72.48, 82.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.40 (-4.69, 9.49)
Absolute Change at Week 24 (MMRM)		
n	28	23
LS mean (SE)	2.91 (2.51)	0.88 (2.76)
95% CI of LS mean	(-2.13, 7.95)	(-4.67, 6.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.03 (-9.56, 5.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	28	25
Mean (SD)	78.49 (12.60)	76.76 (15.87)
Absolute Change at Week 52		
n	27	24
Mean (SD)	5.29 (14.94)	-0.54 (15.04)
Week 52 (MMRM)		
n	28	24
LS mean (SE)	78.33 (2.60)	75.74 (2.82)
95% CI of LS mean	(73.11, 83.54)	(70.06, 81.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.59 (-10.33, 5.15)
Absolute Change at Week 52 (MMRM)		
n	27	23
LS mean (SE)	5.68 (2.87)	-0.56 (3.13)
95% CI of LS mean	(-0.08, 11.43)	(-6.84, 5.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.24 (-14.79, 2.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	28	23
LS mean (SE)	3.24 (2.19)	-0.27 (2.41)
95% CI of LS mean	(-1.16, 7.64)	(-5.12, 4.58)
P-value within Treatment	0.1458	0.9121
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.51 (-10.10, 3.08)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2903
Hedges' G (SE)		-0.30 (0.28)
Hedges' 95% CI		(-0.86, 0.26)
Hedges' P-value		0.2901

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	74.58 (17.51)	74.72 (18.99)
Week 8 (MMRM)		
n	168	164
LS mean (SE)	75.87 (1.34)	75.60 (1.35)
95% CI of LS mean	(73.23, 78.51)	(72.93, 78.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.27 (-4.02, 3.48)
Absolute Change at Week 8 (MMRM)		
n	165	162
LS mean (SE)	1.19 (1.07)	1.18 (1.08)
95% CI of LS mean	(-0.91, 3.30)	(-0.94, 3.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.01 (-3.00, 2.98)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	74.79 (1.47)	74.34 (1.48)
95% CI of LS mean	(71.90, 77.68)	(71.43, 77.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.45 (-4.55, 3.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	0.07 (1.16)	-0.02 (1.17)
95% CI of LS mean	(-2.22, 2.36)	(-2.32, 2.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-3.33, 3.15)
Week 24 (MMRM)		
n	167	164
LS mean (SE)	76.62 (1.38)	76.63 (1.39)
95% CI of LS mean	(73.92, 79.33)	(73.90, 79.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-3.84, 3.85)
Absolute Change at Week 24 (MMRM)		
n	164	162
LS mean (SE)	1.80 (1.03)	2.27 (1.04)
95% CI of LS mean	(-0.22, 3.83)	(0.23, 4.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.46 (-2.42, 3.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	77.58 (16.71)	77.50 (17.78)
Absolute Change at Week 52		
n	162	156
Mean (SD)	2.80 (13.19)	3.21 (14.03)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	77.58 (1.32)	77.87 (1.34)
95% CI of LS mean	(74.98, 80.18)	(75.24, 80.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.29 (-3.41, 3.99)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	2.78 (1.07)	3.33 (1.08)
95% CI of LS mean	(0.68, 4.88)	(1.20, 5.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.55 (-2.45, 3.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	1.55 (0.93)	1.86 (0.93)
95% CI of LS mean	(-0.27, 3.38)	(0.02, 3.69)
P-value within Treatment	0.0954	0.0473
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.31 (-2.28, 2.90)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8161
Hedges' G (SE)		0.03 (0.11)
Hedges' 95% CI		(-0.19, 0.24)
Hedges' P-value		0.8160

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	73.68 (13.96)	71.88 (23.26)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	76.57 (4.36)	77.47 (4.77)
95% CI of LS mean	(67.68, 85.47)	(67.74, 87.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.90 (-12.56, 14.37)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	2.28 (2.34)	6.32 (2.56)
95% CI of LS mean	(-2.50, 7.06)	(1.10, 11.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.04 (-3.13, 11.21)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	73.94 (4.69)	75.04 (5.13)
95% CI of LS mean	(64.34, 83.54)	(64.55, 85.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.10 (-13.37, 15.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-0.35 (2.37)	3.89 (2.59)
95% CI of LS mean	(-5.20, 4.50)	(-1.41, 9.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.24 (-3.03, 11.52)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	76.57 (4.45)	78.17 (4.87)
95% CI of LS mean	(67.49, 85.66)	(68.23, 88.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.60 (-12.14, 15.33)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	2.28 (2.74)	7.02 (2.99)
95% CI of LS mean	(-3.29, 7.85)	(0.93, 13.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.74 (-3.59, 13.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	78.09 (18.42)	72.78 (22.64)
Absolute Change at Week 52		
n	18	13
Mean (SD)	3.70 (10.78)	1.88 (14.01)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	78.33 (4.79)	73.34 (5.41)
95% CI of LS mean	(68.55, 88.11)	(62.33, 84.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.99 (-19.96, 9.97)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	3.85 (2.73)	2.00 (3.24)
95% CI of LS mean	(-1.75, 9.45)	(-4.63, 8.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.85 (-10.59, 6.89)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	1.93 (1.96)	4.30 (2.18)
95% CI of LS mean	(-2.08, 5.93)	(-0.16, 8.76)
P-value within Treatment	0.3341	0.0580
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-3.72, 8.47)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4324
Hedges' G (SE)		0.27 (0.33)
Hedges' 95% CI		(-0.41, 0.95)
Hedges' P-value		0.4253

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	177	174
Mean (SD)	74.35 (17.57)	75.30 (17.91)
Week 8 (MMRM)		
n	178	172
LS mean (SE)	75.49 (1.27)	75.48 (1.29)
95% CI of LS mean	(72.99, 77.99)	(72.95, 78.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.01 (-3.57, 3.55)
Absolute Change at Week 8 (MMRM)		
n	174	170
LS mean (SE)	1.00 (1.06)	0.62 (1.07)
95% CI of LS mean	(-1.08, 3.09)	(-1.50, 2.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.39 (-3.36, 2.58)
Week 16 (MMRM)		
n	177	173
LS mean (SE)	74.97 (1.37)	74.27 (1.38)
95% CI of LS mean	(72.28, 77.66)	(71.55, 76.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.70 (-4.52, 3.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	173	170
LS mean (SE)	0.30 (1.14)	-0.55 (1.15)
95% CI of LS mean	(-1.94, 2.55)	(-2.82, 1.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.86 (-4.05, 2.34)
Week 24 (MMRM)		
n	177	172
LS mean (SE)	76.56 (1.28)	76.47 (1.30)
95% CI of LS mean	(74.04, 79.09)	(73.91, 79.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-3.69, 3.50)
Absolute Change at Week 24 (MMRM)		
n	173	169
LS mean (SE)	1.94 (1.01)	1.63 (1.02)
95% CI of LS mean	(-0.05, 3.93)	(-0.38, 3.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-3.14, 2.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	174	169
Mean (SD)	77.83 (15.87)	77.78 (17.08)
Absolute Change at Week 52		
n	170	166
Mean (SD)	3.25 (13.61)	2.72 (14.26)
Week 52 (MMRM)		
n	173	167
LS mean (SE)	77.75 (1.23)	77.74 (1.25)
95% CI of LS mean	(75.33, 80.17)	(75.28, 80.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.01 (-3.46, 3.44)
Absolute Change at Week 52 (MMRM)		
n	169	164
LS mean (SE)	3.11 (1.07)	2.82 (1.08)
95% CI of LS mean	(1.01, 5.21)	(0.69, 4.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.29 (-3.28, 2.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	173	170
LS mean (SE)	1.78 (0.92)	1.30 (0.93)
95% CI of LS mean	(-0.02, 3.59)	(-0.53, 3.13)
P-value within Treatment	0.0531	0.1632
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.49 (-3.06, 2.09)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7105
Hedges' G (SE)		-0.04 (0.11)
Hedges' 95% CI		(-0.25, 0.17)
Hedges' P-value		0.7104

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	114	115
Mean (SD)	74.86 (18.00)	75.32 (19.28)
Week 8 (MMRM)		
n	116	116
LS mean (SE)	75.52 (1.63)	75.76 (1.64)
95% CI of LS mean	(72.31, 78.74)	(72.54, 78.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.24 (-4.33, 4.81)
Absolute Change at Week 8 (MMRM)		
n	112	115
LS mean (SE)	0.63 (1.24)	0.46 (1.23)
95% CI of LS mean	(-1.81, 3.07)	(-1.95, 2.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-3.61, 3.28)
Week 16 (MMRM)		
n	115	115
LS mean (SE)	74.14 (1.71)	73.90 (1.72)
95% CI of LS mean	(70.76, 77.52)	(70.52, 77.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-5.04, 4.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	111	114
LS mean (SE)	-0.98 (1.37)	-1.42 (1.35)
95% CI of LS mean	(-3.67, 1.71)	(-4.08, 1.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.44 (-4.24, 3.35)
Week 24 (MMRM)		
n	115	115
LS mean (SE)	76.86 (1.64)	77.23 (1.65)
95% CI of LS mean	(73.62, 80.09)	(73.99, 80.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.38 (-4.22, 4.97)
Absolute Change at Week 24 (MMRM)		
n	111	114
LS mean (SE)	1.83 (1.21)	1.94 (1.20)
95% CI of LS mean	(-0.56, 4.22)	(-0.42, 4.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.11 (-3.26, 3.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	113	111
Mean (SD)	77.69 (16.01)	77.23 (18.35)
Absolute Change at Week 52		
n	109	110
Mean (SD)	2.38 (11.20)	1.82 (14.61)
Week 52 (MMRM)		
n	112	111
LS mean (SE)	77.36 (1.60)	77.31 (1.60)
95% CI of LS mean	(74.21, 80.50)	(74.15, 80.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-4.52, 4.42)
Absolute Change at Week 52 (MMRM)		
n	108	110
LS mean (SE)	2.27 (1.25)	1.81 (1.24)
95% CI of LS mean	(-0.20, 4.74)	(-0.64, 4.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.46 (-3.95, 3.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	114
LS mean (SE)	1.04 (1.09)	0.78 (1.08)
95% CI of LS mean	(-1.10, 3.18)	(-1.34, 2.89)
P-value within Treatment	0.3406	0.4716
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-3.29, 2.76)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8639
Hedges' G (SE)		-0.02 (0.13)
Hedges' 95% CI		(-0.28, 0.24)
Hedges' P-value		0.8634

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	77
Mean (SD)	73.47 (16.06)	74.77 (17.03)
Week 8 (MMRM)		
n	81	72
LS mean (SE)	75.24 (1.82)	76.03 (1.92)
95% CI of LS mean	(71.63, 78.84)	(72.23, 79.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.79 (-4.46, 6.03)
Absolute Change at Week 8 (MMRM)		
n	81	71
LS mean (SE)	1.88 (1.63)	2.14 (1.74)
95% CI of LS mean	(-1.34, 5.10)	(-1.29, 5.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.26 (-4.45, 4.98)
Week 16 (MMRM)		
n	81	74
LS mean (SE)	75.47 (2.05)	75.41 (2.14)
95% CI of LS mean	(71.43, 79.51)	(71.19, 79.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-5.91, 5.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	81	72
LS mean (SE)	1.99 (1.66)	1.71 (1.76)
95% CI of LS mean	(-1.29, 5.28)	(-1.78, 5.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.29 (-5.09, 4.51)
Week 24 (MMRM)		
n	81	73
LS mean (SE)	75.72 (1.85)	76.04 (1.94)
95% CI of LS mean	(72.07, 79.37)	(72.21, 79.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.32 (-4.98, 5.62)
Absolute Change at Week 24 (MMRM)		
n	81	71
LS mean (SE)	2.26 (1.55)	2.23 (1.65)
95% CI of LS mean	(-0.81, 5.33)	(-1.04, 5.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-4.52, 4.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	80	73
Mean (SD)	77.74 (16.46)	77.66 (16.22)
Absolute Change at Week 52		
n	80	70
Mean (SD)	4.22 (16.00)	4.10 (13.45)
Week 52 (MMRM)		
n	79	69
LS mean (SE)	78.04 (1.82)	78.07 (1.92)
95% CI of LS mean	(74.45, 81.64)	(74.27, 81.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.03 (-5.21, 5.28)
Absolute Change at Week 52 (MMRM)		
n	79	67
LS mean (SE)	4.58 (1.66)	4.40 (1.79)
95% CI of LS mean	(1.29, 7.86)	(0.87, 7.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-5.00, 4.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	81	72
LS mean (SE)	2.94 (1.38)	2.78 (1.47)
95% CI of LS mean	(0.21, 5.68)	(-0.13, 5.69)
P-value within Treatment	0.0350	0.0609
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.16 (-4.16, 3.84)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9353
Hedges' G (SE)		-0.01 (0.16)
Hedges' 95% CI		(-0.33, 0.31)
Hedges' P-value		0.9352

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	76.70 (15.66)	75.04 (18.41)
Week 8 (MMRM)		
n	88	83
LS mean (SE)	76.76 (1.69)	76.44 (1.73)
95% CI of LS mean	(73.42, 80.09)	(73.02, 79.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-5.09, 4.47)
Absolute Change at Week 8 (MMRM)		
n	86	82
LS mean (SE)	-0.24 (1.37)	1.77 (1.41)
95% CI of LS mean	(-2.95, 2.48)	(-1.01, 4.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.01 (-1.88, 5.90)
Week 16 (MMRM)		
n	89	85
LS mean (SE)	76.96 (1.92)	73.65 (1.96)
95% CI of LS mean	(73.17, 80.74)	(69.78, 77.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.30 (-8.73, 2.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	87	83
LS mean (SE)	-0.26 (1.47)	-0.90 (1.51)
95% CI of LS mean	(-3.17, 2.65)	(-3.88, 2.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-4.81, 3.52)
Week 24 (MMRM)		
n	89	84
LS mean (SE)	78.35 (1.77)	75.34 (1.81)
95% CI of LS mean	(74.85, 81.84)	(71.75, 78.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.01 (-8.02, 2.00)
Absolute Change at Week 24 (MMRM)		
n	87	82
LS mean (SE)	1.42 (1.37)	0.78 (1.40)
95% CI of LS mean	(-1.28, 4.12)	(-1.99, 3.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-4.51, 3.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	88	78
Mean (SD)	78.88 (15.17)	76.72 (16.39)
Absolute Change at Week 52		
n	86	76
Mean (SD)	2.20 (12.58)	2.45 (13.44)
Week 52 (MMRM)		
n	87	77
LS mean (SE)	79.50 (1.64)	76.99 (1.71)
95% CI of LS mean	(76.25, 82.74)	(73.62, 80.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.51 (-7.19, 2.17)
Absolute Change at Week 52 (MMRM)		
n	85	75
LS mean (SE)	2.52 (1.38)	2.39 (1.44)
95% CI of LS mean	(-0.20, 5.23)	(-0.46, 5.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-4.07, 3.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	87	83
LS mean (SE)	1.22 (1.16)	0.75 (1.19)
95% CI of LS mean	(-1.07, 3.52)	(-1.60, 3.11)
P-value within Treatment	0.2928	0.5282
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-3.76, 2.82)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7785
Hedges' G (SE)		-0.04 (0.15)
Hedges' 95% CI		(-0.34, 0.26)
Hedges' P-value		0.7781

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	109	107
Mean (SD)	72.32 (18.15)	75.14 (18.42)
Week 8 (MMRM)		
n	109	105
LS mean (SE)	74.58 (1.73)	75.13 (1.76)
95% CI of LS mean	(71.18, 77.98)	(71.67, 78.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.55 (-4.30, 5.41)
Absolute Change at Week 8 (MMRM)		
n	107	104
LS mean (SE)	2.29 (1.39)	0.52 (1.41)
95% CI of LS mean	(-0.44, 5.03)	(-2.25, 3.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.77 (-5.67, 2.13)
Week 16 (MMRM)		
n	107	104
LS mean (SE)	73.09 (1.80)	74.97 (1.83)
95% CI of LS mean	(69.54, 76.63)	(71.36, 78.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.88 (-3.18, 6.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	105	103
LS mean (SE)	0.71 (1.51)	0.36 (1.52)
95% CI of LS mean	(-2.26, 3.68)	(-2.64, 3.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.35 (-4.58, 3.88)
Week 24 (MMRM)		
n	107	104
LS mean (SE)	75.04 (1.71)	77.71 (1.73)
95% CI of LS mean	(71.67, 78.40)	(74.29, 81.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.67 (-2.13, 7.47)
Absolute Change at Week 24 (MMRM)		
n	105	103
LS mean (SE)	2.49 (1.32)	3.08 (1.34)
95% CI of LS mean	(-0.12, 5.10)	(0.44, 5.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-3.13, 4.30)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	105	106
Mean (SD)	76.73 (16.94)	77.90 (18.32)
Absolute Change at Week 52		
n	103	104
Mean (SD)	3.95 (14.12)	2.89 (14.76)
Week 52 (MMRM)		
n	104	103
LS mean (SE)	76.34 (1.69)	77.84 (1.72)
95% CI of LS mean	(73.00, 79.68)	(74.46, 81.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.50 (-3.25, 6.25)
Absolute Change at Week 52 (MMRM)		
n	102	102
LS mean (SE)	3.84 (1.42)	3.10 (1.43)
95% CI of LS mean	(1.04, 6.64)	(0.29, 5.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.73 (-4.71, 3.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	105	103
LS mean (SE)	2.35 (1.23)	2.18 (1.24)
95% CI of LS mean	(-0.07, 4.76)	(-0.26, 4.62)
P-value within Treatment	0.0569	0.0799
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-3.60, 3.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9241
Hedges' G (SE)		-0.01 (0.14)
Hedges' 95% CI		(-0.29, 0.26)
Hedges' P-value		0.9241

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	111	99
Mean (SD)	70.17 (19.53)	70.03 (18.54)
Week 8 (MMRM)		
n	112	98
LS mean (SE)	68.79 (1.89)	70.13 (2.03)
95% CI of LS mean	(65.06, 72.52)	(66.12, 74.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.34 (-4.15, 6.83)
Absolute Change at Week 8 (MMRM)		
n	109	96
LS mean (SE)	-1.29 (1.16)	0.17 (1.24)
95% CI of LS mean	(-3.58, 1.01)	(-2.28, 2.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.45 (-1.91, 4.82)
Week 16 (MMRM)		
n	113	98
LS mean (SE)	68.78 (1.93)	70.89 (2.07)
95% CI of LS mean	(64.99, 72.58)	(66.81, 74.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.11 (-3.48, 7.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	110	96
LS mean (SE)	-1.70 (1.30)	1.38 (1.39)
95% CI of LS mean	(-4.25, 0.86)	(-1.36, 4.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.07 (-0.68, 6.82)
Week 24 (MMRM)		
n	113	98
LS mean (SE)	71.25 (1.93)	70.55 (2.07)
95% CI of LS mean	(67.45, 75.05)	(66.47, 74.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.70 (-6.29, 4.89)
Absolute Change at Week 24 (MMRM)		
n	110	96
LS mean (SE)	0.83 (1.36)	0.68 (1.46)
95% CI of LS mean	(-1.86, 3.52)	(-2.20, 3.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-4.09, 3.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	112	94
Mean (SD)	71.73 (19.67)	74.11 (19.58)
Absolute Change at Week 52		
n	109	92
Mean (SD)	1.12 (14.10)	4.47 (15.01)
Week 52 (MMRM)		
n	112	93
LS mean (SE)	71.39 (1.84)	73.99 (2.00)
95% CI of LS mean	(67.75, 75.03)	(70.05, 77.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.60 (-2.77, 7.97)
Absolute Change at Week 52 (MMRM)		
n	109	91
LS mean (SE)	0.96 (1.41)	4.12 (1.54)
95% CI of LS mean	(-1.83, 3.75)	(1.09, 7.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.16 (-0.97, 7.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	110	96
LS mean (SE)	0.03 (1.13)	2.06 (1.21)
95% CI of LS mean	(-2.19, 2.25)	(-0.32, 4.44)
P-value within Treatment	0.9793	0.0899
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.03 (-1.24, 5.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2219
Hedges' G (SE)		0.17 (0.14)
Hedges' 95% CI		(-0.10, 0.45)
Hedges' P-value		0.2212

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	85	91
Mean (SD)	70.59 (20.98)	74.36 (20.87)
Week 8 (MMRM)		
n	84	90
LS mean (SE)	73.44 (2.05)	76.50 (1.98)
95% CI of LS mean	(69.39, 77.50)	(72.60, 80.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.06 (-2.58, 8.69)
Absolute Change at Week 8 (MMRM)		
n	83	90
LS mean (SE)	3.00 (1.71)	2.36 (1.64)
95% CI of LS mean	(-0.37, 6.38)	(-0.87, 5.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-5.32, 4.04)
Week 16 (MMRM)		
n	83	91
LS mean (SE)	72.70 (2.27)	75.33 (2.18)
95% CI of LS mean	(68.21, 77.18)	(71.03, 79.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.63 (-3.59, 8.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	82	90
LS mean (SE)	2.28 (1.80)	1.38 (1.72)
95% CI of LS mean	(-1.27, 5.83)	(-2.02, 4.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.90 (-5.82, 4.03)
Week 24 (MMRM)		
n	83	90
LS mean (SE)	73.64 (2.18)	75.92 (2.09)
95% CI of LS mean	(69.33, 77.94)	(71.78, 80.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.28 (-3.69, 8.25)
Absolute Change at Week 24 (MMRM)		
n	82	89
LS mean (SE)	3.28 (1.59)	1.69 (1.53)
95% CI of LS mean	(0.14, 6.42)	(-1.32, 4.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.58 (-5.94, 2.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	80	87
Mean (SD)	76.53 (20.16)	78.54 (18.23)
Absolute Change at Week 52		
n	79	86
Mean (SD)	6.19 (18.03)	4.52 (16.11)
Week 52 (MMRM)		
n	79	87
LS mean (SE)	75.96 (2.13)	78.78 (2.04)
95% CI of LS mean	(71.75, 80.17)	(74.75, 82.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.82 (-3.01, 8.65)
Absolute Change at Week 52 (MMRM)		
n	78	86
LS mean (SE)	5.46 (1.90)	4.47 (1.81)
95% CI of LS mean	(1.72, 9.21)	(0.89, 8.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.99 (-6.18, 4.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	82	90
LS mean (SE)	3.67 (1.55)	2.52 (1.48)
95% CI of LS mean	(0.62, 6.73)	(-0.41, 5.44)
P-value within Treatment	0.0186	0.0915
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.16 (-5.39, 3.07)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5900
Hedges' G (SE)		-0.08 (0.15)
Hedges' 95% CI		(-0.38, 0.22)
Hedges' P-value		0.5899

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	29	25
Mean (SD)	70.11 (19.04)	72.89 (22.70)
Week 8 (MMRM)		
n	29	24
LS mean (SE)	69.45 (3.40)	77.03 (3.73)
95% CI of LS mean	(62.62, 76.28)	(69.53, 84.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.58 (-2.62, 17.78)
Absolute Change at Week 8 (MMRM)		
n	28	24
LS mean (SE)	-1.16 (3.59)	6.62 (3.92)
95% CI of LS mean	(-8.38, 6.05)	(-1.26, 14.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.79 (-2.95, 18.52)
Week 16 (MMRM)		
n	29	24
LS mean (SE)	68.41 (4.07)	76.01 (4.48)
95% CI of LS mean	(60.23, 76.59)	(67.02, 85.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.60 (-4.60, 19.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	28	23
LS mean (SE)	-3.07 (4.08)	6.53 (4.49)
95% CI of LS mean	(-11.26, 5.13)	(-2.49, 15.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.60 (-2.64, 21.83)
Week 24 (MMRM)		
n	29	24
LS mean (SE)	71.70 (3.81)	74.75 (4.19)
95% CI of LS mean	(64.05, 79.34)	(66.34, 83.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.05 (-8.38, 14.48)
Absolute Change at Week 24 (MMRM)		
n	28	23
LS mean (SE)	0.89 (3.72)	4.37 (4.11)
95% CI of LS mean	(-6.60, 8.37)	(-3.89, 12.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.48 (-7.72, 14.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	28	25
Mean (SD)	72.62 (19.24)	80.00 (18.98)
Absolute Change at Week 52		
n	27	24
Mean (SD)	2.47 (19.57)	7.87 (26.11)
Week 52 (MMRM)		
n	28	24
LS mean (SE)	72.63 (3.58)	78.91 (3.91)
95% CI of LS mean	(65.44, 79.82)	(71.06, 86.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.28 (-4.42, 16.98)
Absolute Change at Week 52 (MMRM)		
n	27	23
LS mean (SE)	1.72 (4.34)	7.98 (4.75)
95% CI of LS mean	(-6.99, 10.43)	(-1.56, 17.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.26 (-6.70, 19.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	28	23
LS mean (SE)	-0.15 (3.59)	6.29 (3.96)
95% CI of LS mean	(-7.37, 7.07)	(-1.65, 14.24)
P-value within Treatment	0.9665	0.1180
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.45 (-4.34, 17.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2358
Hedges' G (SE)		0.33 (0.28)
Hedges' 95% CI		(-0.23, 0.89)
Hedges' P-value		0.2369

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	70.44 (20.30)	72.19 (19.36)
Week 8 (MMRM)		
n	167	164
LS mean (SE)	71.14 (1.51)	72.52 (1.53)
95% CI of LS mean	(68.16, 74.12)	(69.52, 75.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.39 (-2.85, 5.62)
Absolute Change at Week 8 (MMRM)		
n	164	162
LS mean (SE)	0.85 (0.99)	0.45 (0.99)
95% CI of LS mean	(-1.09, 2.80)	(-1.51, 2.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.41 (-3.17, 2.35)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	70.93 (1.57)	72.46 (1.58)
95% CI of LS mean	(67.85, 74.01)	(69.36, 75.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.53 (-2.85, 5.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	0.55 (1.05)	0.62 (1.06)
95% CI of LS mean	(-1.52, 2.62)	(-1.46, 2.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-2.87, 3.00)
Week 24 (MMRM)		
n	167	164
LS mean (SE)	72.47 (1.56)	72.76 (1.57)
95% CI of LS mean	(69.40, 75.54)	(69.66, 75.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.29 (-4.07, 4.65)
Absolute Change at Week 24 (MMRM)		
n	164	162
LS mean (SE)	2.05 (1.05)	0.70 (1.06)
95% CI of LS mean	(-0.02, 4.11)	(-1.38, 2.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.35 (-4.28, 1.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	73.87 (20.08)	75.75 (18.95)
Absolute Change at Week 52		
n	162	156
Mean (SD)	3.29 (15.41)	3.92 (13.10)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	73.58 (1.51)	75.79 (1.53)
95% CI of LS mean	(70.60, 76.56)	(72.77, 78.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.20 (-2.03, 6.44)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	3.12 (1.14)	3.73 (1.15)
95% CI of LS mean	(0.88, 5.36)	(1.46, 6.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.61 (-2.58, 3.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	1.91 (0.91)	1.68 (0.91)
95% CI of LS mean	(0.12, 3.69)	(-0.11, 3.48)
P-value within Treatment	0.0365	0.0664
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-2.76, 2.31)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8622
Hedges' G (SE)		-0.02 (0.11)
Hedges' 95% CI		(-0.24, 0.20)
Hedges' P-value		0.8621

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	70.18 (18.90)	72.92 (15.70)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	75.53 (4.10)	70.73 (4.49)
95% CI of LS mean	(67.15, 83.91)	(61.56, 79.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.80 (-17.50, 7.89)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	5.13 (2.49)	-1.93 (2.72)
95% CI of LS mean	(0.06, 10.20)	(-7.46, 3.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.06 (-14.66, 0.55)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	70.27 (4.48)	66.56 (4.90)
95% CI of LS mean	(61.12, 79.42)	(56.56, 76.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.71 (-17.51, 10.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-0.13 (3.13)	-6.09 (3.42)
95% CI of LS mean	(-6.51, 6.24)	(-13.05, 0.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.96 (-15.46, 3.55)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	74.36 (4.46)	67.95 (4.88)
95% CI of LS mean	(65.26, 83.46)	(58.00, 77.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.41 (-20.15, 7.32)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	3.96 (3.12)	-4.70 (3.40)
95% CI of LS mean	(-2.38, 10.30)	(-11.62, 2.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.66 (-18.12, 0.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	74.69 (18.98)	68.25 (20.37)
Absolute Change at Week 52		
n	18	13
Mean (SD)	4.32 (6.75)	-3.42 (13.13)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	73.86 (4.70)	67.39 (5.32)
95% CI of LS mean	(64.26, 83.46)	(56.56, 78.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.47 (-21.17, 8.23)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	3.91 (2.38)	-3.60 (2.84)
95% CI of LS mean	(-0.96, 8.78)	(-9.42, 2.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.52 (-15.15, 0.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	2.58 (2.19)	-4.80 (2.43)
95% CI of LS mean	(-1.94, 7.10)	(-9.79, 0.19)
P-value within Treatment	0.2504	0.0588
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.38 (-14.21, -0.55)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0352
Hedges' G (SE)		-0.75 (0.34)
Hedges' 95% CI		(-1.45, -0.05)
Hedges' P-value		0.0364

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	177	174
Mean (SD)	70.31 (20.26)	72.29 (20.19)
Week 8 (MMRM)		
n	177	172
LS mean (SE)	70.43 (1.47)	73.26 (1.49)
95% CI of LS mean	(67.53, 73.33)	(70.32, 76.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.83 (-1.30, 6.96)
Absolute Change at Week 8 (MMRM)		
n	173	170
LS mean (SE)	0.07 (1.07)	1.48 (1.08)
95% CI of LS mean	(-2.03, 2.17)	(-0.64, 3.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.41 (-1.57, 4.39)
Week 16 (MMRM)		
n	177	173
LS mean (SE)	70.63 (1.55)	73.47 (1.57)
95% CI of LS mean	(67.59, 73.68)	(70.39, 76.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.84 (-1.50, 7.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	173	170
LS mean (SE)	0.09 (1.13)	2.04 (1.14)
95% CI of LS mean	(-2.14, 2.32)	(-0.21, 4.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.95 (-1.22, 5.12)
Week 24 (MMRM)		
n	177	172
LS mean (SE)	72.21 (1.52)	73.44 (1.54)
95% CI of LS mean	(69.21, 75.21)	(70.41, 76.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.23 (-3.04, 5.50)
Absolute Change at Week 24 (MMRM)		
n	173	169
LS mean (SE)	1.70 (1.10)	1.67 (1.11)
95% CI of LS mean	(-0.45, 3.86)	(-0.51, 3.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-3.10, 3.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	174	169
Mean (SD)	73.44 (20.02)	76.92 (18.78)
Absolute Change at Week 52		
n	170	166
Mean (SD)	3.01 (16.74)	5.02 (15.50)
Week 52 (MMRM)		
n	173	167
LS mean (SE)	73.43 (1.46)	76.88 (1.48)
95% CI of LS mean	(70.56, 76.30)	(73.97, 79.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.45 (-0.64, 7.54)
Absolute Change at Week 52 (MMRM)		
n	169	164
LS mean (SE)	2.88 (1.23)	5.05 (1.24)
95% CI of LS mean	(0.47, 5.30)	(2.60, 7.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.17 (-1.27, 5.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	173	170
LS mean (SE)	1.56 (0.98)	2.92 (0.99)
95% CI of LS mean	(-0.38, 3.49)	(0.96, 4.87)
P-value within Treatment	0.1143	0.0036
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.36 (-1.39, 4.11)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3320
Hedges' G (SE)		0.10 (0.11)
Hedges' 95% CI		(-0.11, 0.32)
Hedges' P-value		0.3321

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	114	115
Mean (SD)	71.73 (20.86)	73.53 (20.10)
Week 8 (MMRM)		
n	115	116
LS mean (SE)	71.49 (1.83)	73.68 (1.84)
95% CI of LS mean	(67.88, 75.11)	(70.07, 77.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.19 (-2.94, 7.32)
Absolute Change at Week 8 (MMRM)		
n	111	115
LS mean (SE)	-0.21 (1.25)	0.23 (1.24)
95% CI of LS mean	(-2.68, 2.26)	(-2.21, 2.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.44 (-3.04, 3.92)
Week 16 (MMRM)		
n	115	115
LS mean (SE)	71.89 (1.88)	74.42 (1.89)
95% CI of LS mean	(68.18, 75.59)	(70.70, 78.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.53 (-2.74, 7.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	111	114
LS mean (SE)	-0.15 (1.33)	1.09 (1.32)
95% CI of LS mean	(-2.77, 2.48)	(-1.50, 3.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.24 (-2.46, 4.94)
Week 24 (MMRM)		
n	115	115
LS mean (SE)	72.87 (1.87)	74.62 (1.87)
95% CI of LS mean	(69.20, 76.55)	(70.93, 78.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.74 (-3.48, 6.97)
Absolute Change at Week 24 (MMRM)		
n	111	114
LS mean (SE)	0.87 (1.33)	1.30 (1.32)
95% CI of LS mean	(-1.76, 3.49)	(-1.30, 3.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-3.27, 4.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	113	111
Mean (SD)	74.73 (21.63)	76.18 (19.87)
Absolute Change at Week 52		
n	109	110
Mean (SD)	2.34 (15.43)	3.03 (14.89)
Week 52 (MMRM)		
n	112	111
LS mean (SE)	74.25 (1.94)	76.41 (1.94)
95% CI of LS mean	(70.43, 78.06)	(72.59, 80.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.17 (-3.25, 7.59)
Absolute Change at Week 52 (MMRM)		
n	108	110
LS mean (SE)	2.19 (1.45)	3.11 (1.44)
95% CI of LS mean	(-0.66, 5.05)	(0.28, 5.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.91 (-3.12, 4.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	114
LS mean (SE)	0.97 (1.17)	1.83 (1.16)
95% CI of LS mean	(-1.34, 3.28)	(-0.45, 4.11)
P-value within Treatment	0.4077	0.1150
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.86 (-2.40, 4.12)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6031
Hedges' G (SE)		0.07 (0.13)
Hedges' 95% CI		(-0.19, 0.33)
Hedges' P-value		0.6019

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	77
Mean (SD)	68.54 (18.92)	70.42 (19.21)
Week 8 (MMRM)		
n	81	72
LS mean (SE)	70.20 (2.12)	72.02 (2.23)
95% CI of LS mean	(66.01, 74.39)	(67.62, 76.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.82 (-4.27, 7.91)
Absolute Change at Week 8 (MMRM)		
n	81	71
LS mean (SE)	1.87 (1.64)	2.52 (1.75)
95% CI of LS mean	(-1.37, 5.11)	(-0.93, 5.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.65 (-4.09, 5.39)
Week 16 (MMRM)		
n	81	74
LS mean (SE)	68.87 (2.32)	70.40 (2.43)
95% CI of LS mean	(64.28, 73.46)	(65.60, 75.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.53 (-5.12, 8.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	81	72
LS mean (SE)	0.56 (1.80)	1.49 (1.91)
95% CI of LS mean	(-2.99, 4.12)	(-2.28, 5.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (-4.27, 6.12)
Week 24 (MMRM)		
n	81	73
LS mean (SE)	71.87 (2.24)	70.29 (2.35)
95% CI of LS mean	(67.45, 76.30)	(65.64, 74.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.59 (-8.02, 4.84)
Absolute Change at Week 24 (MMRM)		
n	81	71
LS mean (SE)	3.59 (1.64)	0.57 (1.74)
95% CI of LS mean	(0.36, 6.82)	(-2.87, 4.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.02 (-7.75, 1.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	80	73
Mean (SD)	72.22 (17.23)	76.56 (17.62)
Absolute Change at Week 52		
n	80	70
Mean (SD)	4.31 (16.82)	6.67 (16.10)
Week 52 (MMRM)		
n	79	69
LS mean (SE)	72.38 (1.93)	75.71 (2.04)
95% CI of LS mean	(68.56, 76.21)	(71.67, 79.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.33 (-2.25, 8.90)
Absolute Change at Week 52 (MMRM)		
n	79	67
LS mean (SE)	4.17 (1.87)	5.86 (2.01)
95% CI of LS mean	(0.47, 7.87)	(1.89, 9.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.69 (-3.75, 7.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	81	72
LS mean (SE)	2.78 (1.51)	2.64 (1.61)
95% CI of LS mean	(-0.21, 5.76)	(-0.54, 5.82)
P-value within Treatment	0.0684	0.1027
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-4.51, 4.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9515
Hedges' G (SE)		-0.01 (0.16)
Hedges' 95% CI		(-0.33, 0.31)
Hedges' P-value		0.9514

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	69.70 (18.81)	72.16 (18.28)
Week 8 (MMRM)		
n	88	83
LS mean (SE)	71.34 (1.98)	72.74 (2.03)
95% CI of LS mean	(67.44, 75.24)	(68.74, 76.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.40 (-4.19, 7.00)
Absolute Change at Week 8 (MMRM)		
n	86	82
LS mean (SE)	1.61 (1.29)	0.67 (1.32)
95% CI of LS mean	(-0.93, 4.16)	(-1.94, 3.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.95 (-4.60, 2.70)
Week 16 (MMRM)		
n	89	85
LS mean (SE)	71.30 (2.24)	71.89 (2.29)
95% CI of LS mean	(66.87, 75.72)	(67.36, 76.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.59 (-5.75, 6.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	87	83
LS mean (SE)	1.29 (1.55)	0.25 (1.59)
95% CI of LS mean	(-1.78, 4.36)	(-2.89, 3.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.04 (-5.44, 3.36)
Week 24 (MMRM)		
n	89	84
LS mean (SE)	72.29 (2.07)	71.53 (2.12)
95% CI of LS mean	(68.21, 76.38)	(67.34, 75.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.76 (-6.62, 5.10)
Absolute Change at Week 24 (MMRM)		
n	87	82
LS mean (SE)	2.44 (1.48)	-0.43 (1.52)
95% CI of LS mean	(-0.47, 5.36)	(-3.42, 2.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.87 (-7.05, 1.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	88	78
Mean (SD)	75.25 (18.59)	74.93 (18.47)
Absolute Change at Week 52		
n	86	76
Mean (SD)	5.81 (15.50)	3.22 (12.28)
Week 52 (MMRM)		
n	87	77
LS mean (SE)	75.33 (1.96)	74.80 (2.03)
95% CI of LS mean	(71.46, 79.19)	(70.79, 78.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.53 (-6.10, 5.04)
Absolute Change at Week 52 (MMRM)		
n	85	75
LS mean (SE)	5.54 (1.55)	2.86 (1.63)
95% CI of LS mean	(2.48, 8.61)	(-0.35, 6.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.68 (-7.13, 1.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	87	83
LS mean (SE)	3.09 (1.27)	0.90 (1.31)
95% CI of LS mean	(0.59, 5.60)	(-1.68, 3.47)
P-value within Treatment	0.0159	0.4930
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.19 (-5.79, 1.40)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2303
Hedges' G (SE)		-0.18 (0.15)
Hedges' 95% CI		(-0.49, 0.12)
Hedges' P-value		0.2305

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	109	107
Mean (SD)	70.95 (21.11)	72.38 (20.95)
Week 8 (MMRM)		
n	108	105
LS mean (SE)	70.42 (1.94)	73.45 (1.97)
95% CI of LS mean	(66.60, 74.25)	(69.56, 77.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.03 (-2.43, 8.49)
Absolute Change at Week 8 (MMRM)		
n	106	104
LS mean (SE)	-0.34 (1.46)	1.63 (1.48)
95% CI of LS mean	(-3.22, 2.55)	(-1.29, 4.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.97 (-2.14, 6.07)
Week 16 (MMRM)		
n	107	104
LS mean (SE)	69.90 (1.93)	73.83 (1.97)
95% CI of LS mean	(66.09, 73.71)	(69.96, 77.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.93 (-1.50, 9.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	105	103
LS mean (SE)	-0.99 (1.47)	2.24 (1.49)
95% CI of LS mean	(-3.89, 1.91)	(-0.70, 5.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.23 (-0.90, 7.35)
Week 24 (MMRM)		
n	107	104
LS mean (SE)	72.40 (2.00)	74.26 (2.03)
95% CI of LS mean	(68.46, 76.34)	(70.25, 78.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.86 (-3.76, 7.48)
Absolute Change at Week 24 (MMRM)		
n	105	103
LS mean (SE)	1.46 (1.45)	2.37 (1.46)
95% CI of LS mean	(-1.39, 4.31)	(-0.51, 5.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.91 (-3.14, 4.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	105	106
Mean (SD)	72.38 (20.96)	77.36 (19.33)
Absolute Change at Week 52		
n	103	104
Mean (SD)	0.97 (16.18)	5.34 (17.38)
Week 52 (MMRM)		
n	104	103
LS mean (SE)	71.78 (1.95)	77.34 (1.98)
95% CI of LS mean	(67.93, 75.64)	(73.44, 81.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.56 (0.07, 11.05)
Absolute Change at Week 52 (MMRM)		
n	102	102
LS mean (SE)	0.76 (1.64)	5.37 (1.65)
95% CI of LS mean	(-2.48, 4.00)	(2.11, 8.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.61 (0.01, 9.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	105	103
LS mean (SE)	0.41 (1.32)	3.33 (1.33)
95% CI of LS mean	(-2.19, 3.01)	(0.70, 5.95)
P-value within Treatment	0.7550	0.0134
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.91 (-0.78, 6.61)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1217
Hedges' G (SE)		0.21 (0.14)
Hedges' 95% CI		(-0.06, 0.49)
Hedges' P-value		0.1228

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	108	99
Mean (SD)	66.74 (18.49)	67.68 (20.46)
Week 8 (MMRM)		
n	109	98
LS mean (SE)	64.19 (1.89)	68.44 (1.99)
95% CI of LS mean	(60.47, 67.91)	(64.52, 72.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.25 (-1.16, 9.67)
Absolute Change at Week 8 (MMRM)		
n	107	96
LS mean (SE)	-2.96 (1.72)	0.69 (1.81)
95% CI of LS mean	(-6.34, 0.43)	(-2.89, 4.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.64 (-1.29, 8.57)
Week 16 (MMRM)		
n	109	98
LS mean (SE)	64.28 (1.97)	68.82 (2.08)
95% CI of LS mean	(60.40, 68.16)	(64.72, 72.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.54 (-1.11, 10.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	107	96
LS mean (SE)	-2.58 (1.53)	1.49 (1.62)
95% CI of LS mean	(-5.59, 0.44)	(-1.69, 4.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.07 (-0.32, 8.47)
Week 24 (MMRM)		
n	109	98
LS mean (SE)	64.02 (2.10)	66.11 (2.21)
95% CI of LS mean	(59.89, 68.16)	(61.75, 70.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.08 (-3.94, 8.11)
Absolute Change at Week 24 (MMRM)		
n	107	96
LS mean (SE)	-3.04 (1.62)	-1.88 (1.71)
95% CI of LS mean	(-6.24, 0.16)	(-5.26, 1.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.16 (-3.50, 5.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	108	94
Mean (SD)	66.28 (18.87)	68.17 (20.00)
Absolute Change at Week 52		
n	106	92
Mean (SD)	-1.34 (13.71)	0.63 (16.86)
Week 52 (MMRM)		
n	108	93
LS mean (SE)	65.99 (1.84)	68.64 (1.96)
95% CI of LS mean	(62.36, 69.62)	(64.76, 72.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.65 (-2.67, 7.97)
Absolute Change at Week 52 (MMRM)		
n	106	91
LS mean (SE)	-1.18 (1.50)	0.60 (1.61)
95% CI of LS mean	(-4.13, 1.77)	(-2.57, 3.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.78 (-2.56, 6.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	107	96
LS mean (SE)	-2.27 (1.25)	0.07 (1.32)
95% CI of LS mean	(-4.72, 0.19)	(-2.53, 2.67)
P-value within Treatment	0.0704	0.9561
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.34 (-1.25, 5.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2003
Hedges' G (SE)		0.18 (0.14)
Hedges' 95% CI		(-0.10, 0.46)
Hedges' P-value		0.1997

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	80	86
Mean (SD)	66.84 (16.83)	71.41 (19.45)
Week 8 (MMRM)		
n	80	85
LS mean (SE)	66.12 (2.16)	67.21 (2.09)
95% CI of LS mean	(61.85, 70.38)	(63.08, 71.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.09 (-4.85, 7.03)
Absolute Change at Week 8 (MMRM)		
n	79	85
LS mean (SE)	-0.77 (1.92)	-4.28 (1.85)
95% CI of LS mean	(-4.56, 3.02)	(-7.92, -0.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.51 (-8.77, 1.75)
Week 16 (MMRM)		
n	78	86
LS mean (SE)	64.99 (2.28)	66.69 (2.18)
95% CI of LS mean	(60.49, 69.49)	(62.38, 71.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.71 (-4.53, 7.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	77	86
LS mean (SE)	-1.76 (1.92)	-4.79 (1.82)
95% CI of LS mean	(-5.55, 2.03)	(-8.39, -1.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.03 (-8.26, 2.20)
Week 24 (MMRM)		
n	78	85
LS mean (SE)	64.54 (2.17)	69.37 (2.08)
95% CI of LS mean	(60.25, 68.83)	(65.25, 73.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.83 (-1.12, 10.77)
Absolute Change at Week 24 (MMRM)		
n	77	85
LS mean (SE)	-2.20 (1.91)	-2.17 (1.82)
95% CI of LS mean	(-5.97, 1.58)	(-5.76, 1.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.02 (-5.19, 5.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	75	82
Mean (SD)	67.78 (18.45)	69.31 (20.15)
Absolute Change at Week 52		
n	74	82
Mean (SD)	1.28 (16.44)	-2.03 (19.67)
Week 52 (MMRM)		
n	74	82
LS mean (SE)	67.70 (2.22)	69.57 (2.13)
95% CI of LS mean	(63.30, 72.09)	(65.37, 73.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.87 (-4.21, 7.96)
Absolute Change at Week 52 (MMRM)		
n	73	82
LS mean (SE)	0.79 (2.08)	-1.92 (1.97)
95% CI of LS mean	(-3.32, 4.89)	(-5.81, 1.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.70 (-8.37, 2.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	77	86
LS mean (SE)	-1.06 (1.63)	-2.96 (1.56)
95% CI of LS mean	(-4.28, 2.17)	(-6.03, 0.11)
P-value within Treatment	0.5190	0.0590
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.90 (-6.36, 2.55)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4005
Hedges' G (SE)		-0.13 (0.16)
Hedges' 95% CI		(-0.44, 0.18)
Hedges' P-value		0.4008

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	21	20
Mean (SD)	66.27 (16.97)	72.08 (19.36)
Week 8 (MMRM)		
n	21	19
LS mean (SE)	68.89 (3.71)	72.10 (3.90)
95% CI of LS mean	(61.37, 76.42)	(64.19, 80.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.21 (-7.74, 14.16)
Absolute Change at Week 8 (MMRM)		
n	21	19
LS mean (SE)	3.12 (3.75)	0.94 (3.94)
95% CI of LS mean	(-4.49, 10.72)	(-7.05, 8.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.17 (-13.23, 8.89)
Week 16 (MMRM)		
n	20	19
LS mean (SE)	65.86 (4.35)	65.52 (4.50)
95% CI of LS mean	(57.04, 74.68)	(56.41, 74.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.34 (-13.05, 12.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	20	19
LS mean (SE)	0.27 (4.08)	-5.64 (4.21)
95% CI of LS mean	(-7.99, 8.53)	(-14.16, 2.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.90 (-17.80, 5.99)
Week 24 (MMRM)		
n	20	19
LS mean (SE)	63.74 (3.78)	72.54 (3.90)
95% CI of LS mean	(56.07, 71.40)	(64.63, 80.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.80 (-2.25, 19.85)
Absolute Change at Week 24 (MMRM)		
n	20	19
LS mean (SE)	-1.79 (3.35)	1.38 (3.45)
95% CI of LS mean	(-8.58, 5.00)	(-5.62, 8.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.17 (-6.62, 12.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	19	20
Mean (SD)	64.04 (22.40)	72.92 (19.28)
Absolute Change at Week 52		
n	19	20
Mean (SD)	-2.63 (17.14)	0.83 (18.91)
Week 52 (MMRM)		
n	19	19
LS mean (SE)	63.71 (4.68)	71.66 (4.75)
95% CI of LS mean	(54.23, 73.20)	(62.03, 81.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.95 (-5.59, 21.49)
Absolute Change at Week 52 (MMRM)		
n	19	19
LS mean (SE)	-2.11 (4.20)	0.50 (4.24)
95% CI of LS mean	(-10.62, 6.40)	(-8.10, 9.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.62 (-9.51, 14.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	20	19
LS mean (SE)	-1.21 (3.07)	-1.25 (3.17)
95% CI of LS mean	(-7.44, 5.02)	(-7.68, 5.18)
P-value within Treatment	0.6956	0.6956
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-9.03, 8.95)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9933
Hedges' G (SE)		0.00 (0.31)
Hedges' 95% CI		(-0.64, 0.63)
Hedges' P-value		0.9932

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	66.85 (17.85)	69.36 (20.19)
Week 8 (MMRM)		
n	168	164
LS mean (SE)	64.54 (1.51)	67.37 (1.53)
95% CI of LS mean	(61.56, 67.52)	(64.36, 70.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.82 (-1.41, 7.06)
Absolute Change at Week 8 (MMRM)		
n	165	162
LS mean (SE)	-2.63 (1.37)	-1.98 (1.38)
95% CI of LS mean	(-5.33, 0.06)	(-4.70, 0.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.65 (-3.17, 4.48)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	64.44 (1.59)	68.04 (1.60)
95% CI of LS mean	(61.32, 67.56)	(64.90, 71.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.60 (-0.82, 8.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	-2.51 (1.25)	-1.02 (1.26)
95% CI of LS mean	(-4.97, -0.05)	(-3.49, 1.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.49 (-2.00, 4.97)
Week 24 (MMRM)		
n	167	164
LS mean (SE)	64.34 (1.63)	67.00 (1.65)
95% CI of LS mean	(61.12, 67.55)	(63.75, 70.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.66 (-1.91, 7.23)
Absolute Change at Week 24 (MMRM)		
n	164	162
LS mean (SE)	-2.76 (1.32)	-2.47 (1.33)
95% CI of LS mean	(-5.35, -0.17)	(-5.08, 0.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.29 (-3.39, 3.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	67.22 (18.18)	68.45 (20.12)
Absolute Change at Week 52		
n	162	156
Mean (SD)	0.02 (14.61)	-0.80 (18.08)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	67.08 (1.48)	68.73 (1.50)
95% CI of LS mean	(64.16, 70.00)	(65.77, 71.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.65 (-2.51, 5.80)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	-0.09 (1.30)	-0.79 (1.32)
95% CI of LS mean	(-2.65, 2.46)	(-3.38, 1.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.69 (-4.33, 2.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	-1.79 (1.06)	-1.43 (1.06)
95% CI of LS mean	(-3.86, 0.29)	(-3.52, 0.67)
P-value within Treatment	0.0918	0.1808
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-2.59, 3.31)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8099
Hedges' G (SE)		0.03 (0.11)
Hedges' 95% CI		(-0.19, 0.24)
Hedges' P-value		0.8098

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	69.30 (20.23)	59.90 (26.91)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	69.03 (4.46)	65.43 (4.87)
95% CI of LS mean	(59.94, 78.12)	(55.50, 75.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.60 (-17.25, 10.05)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	0.12 (4.13)	5.07 (4.51)
95% CI of LS mean	(-8.29, 8.52)	(-4.11, 14.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.95 (-7.63, 17.53)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	64.64 (5.04)	64.39 (5.51)
95% CI of LS mean	(54.36, 74.92)	(53.16, 75.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-15.64, 15.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-4.27 (5.18)	4.03 (5.65)
95% CI of LS mean	(-14.81, 6.27)	(-7.47, 15.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.30 (-7.41, 24.00)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	69.03 (4.36)	62.82 (4.76)
95% CI of LS mean	(60.12, 77.93)	(53.10, 72.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.20 (-19.58, 7.17)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	0.12 (4.43)	2.47 (4.84)
95% CI of LS mean	(-8.92, 9.15)	(-7.40, 12.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.35 (-11.15, 15.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	76.39 (19.23)	60.71 (18.90)
Absolute Change at Week 52		
n	18	13
Mean (SD)	6.02 (13.65)	3.85 (18.82)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	75.89 (4.51)	61.10 (5.30)
95% CI of LS mean	(66.66, 85.12)	(50.27, 71.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-14.79 (-29.16, -0.42)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	6.31 (3.60)	3.36 (4.27)
95% CI of LS mean	(-1.06, 13.68)	(-5.38, 12.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.95 (-14.47, 8.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	0.72 (3.48)	3.28 (3.84)
95% CI of LS mean	(-6.39, 7.83)	(-4.56, 11.13)
P-value within Treatment	0.8377	0.3993
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.57 (-8.16, 13.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6289
Hedges' G (SE)		0.16 (0.33)
Hedges' 95% CI		(-0.51, 0.84)
Hedges' P-value		0.6240

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	169	169
Mean (SD)	66.55 (17.49)	70.76 (19.05)
Week 8 (MMRM)		
n	170	167
LS mean (SE)	64.57 (1.49)	68.10 (1.50)
95% CI of LS mean	(61.64, 67.51)	(65.14, 71.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.52 (-0.64, 7.68)
Absolute Change at Week 8 (MMRM)		
n	167	165
LS mean (SE)	-2.26 (1.35)	-2.30 (1.36)
95% CI of LS mean	(-4.91, 0.40)	(-4.96, 0.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-3.80, 3.72)
Week 16 (MMRM)		
n	168	168
LS mean (SE)	64.59 (1.56)	68.11 (1.57)
95% CI of LS mean	(61.52, 67.67)	(65.03, 71.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.52 (-0.84, 7.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	165	166
LS mean (SE)	-1.98 (1.21)	-2.01 (1.20)
95% CI of LS mean	(-4.35, 0.40)	(-4.38, 0.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-3.39, 3.32)
Week 24 (MMRM)		
n	168	167
LS mean (SE)	63.75 (1.61)	68.03 (1.62)
95% CI of LS mean	(60.58, 66.92)	(64.85, 71.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.28 (-0.22, 8.78)
Absolute Change at Week 24 (MMRM)		
n	165	165
LS mean (SE)	-2.99 (1.27)	-2.48 (1.27)
95% CI of LS mean	(-5.49, -0.48)	(-4.98, 0.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.51 (-3.03, 4.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	165	164
Mean (SD)	65.91 (18.35)	69.92 (19.77)
Absolute Change at Week 52		
n	162	162
Mean (SD)	-0.96 (14.91)	-0.93 (18.13)
Week 52 (MMRM)		
n	164	162
LS mean (SE)	65.75 (1.48)	69.70 (1.49)
95% CI of LS mean	(62.84, 68.66)	(66.78, 72.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.96 (-0.17, 8.08)
Absolute Change at Week 52 (MMRM)		
n	161	160
LS mean (SE)	-1.08 (1.31)	-0.89 (1.32)
95% CI of LS mean	(-3.66, 1.50)	(-3.48, 1.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.19 (-3.47, 3.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	165	166
LS mean (SE)	-2.01 (1.03)	-1.79 (1.03)
95% CI of LS mean	(-4.05, 0.02)	(-3.83, 0.24)
P-value within Treatment	0.0523	0.0841
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.22 (-2.66, 3.10)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8791
Hedges' G (SE)		0.02 (0.11)
Hedges' 95% CI		(-0.20, 0.23)
Hedges' P-value		0.8789

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	109	114
Mean (SD)	67.79 (18.86)	72.08 (18.88)
Week 8 (MMRM)		
n	110	115
LS mean (SE)	66.53 (1.84)	69.21 (1.81)
95% CI of LS mean	(62.89, 70.16)	(65.65, 72.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.68 (-2.42, 7.78)
Absolute Change at Week 8 (MMRM)		
n	107	114
LS mean (SE)	-1.73 (1.65)	-2.65 (1.60)
95% CI of LS mean	(-4.98, 1.52)	(-5.80, 0.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.92 (-5.46, 3.62)
Week 16 (MMRM)		
n	109	115
LS mean (SE)	66.07 (1.93)	69.50 (1.88)
95% CI of LS mean	(62.26, 69.87)	(65.78, 73.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.43 (-1.89, 8.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	106	114
LS mean (SE)	-1.85 (1.50)	-2.36 (1.45)
95% CI of LS mean	(-4.81, 1.11)	(-5.21, 0.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.50 (-4.62, 3.62)
Week 24 (MMRM)		
n	109	115
LS mean (SE)	66.60 (1.94)	69.57 (1.89)
95% CI of LS mean	(62.78, 70.42)	(65.84, 73.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.97 (-2.38, 8.31)
Absolute Change at Week 24 (MMRM)		
n	106	114
LS mean (SE)	-1.54 (1.51)	-2.28 (1.46)
95% CI of LS mean	(-4.52, 1.44)	(-5.16, 0.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.74 (-4.89, 3.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	107	111
Mean (SD)	68.77 (18.74)	69.67 (20.44)
Absolute Change at Week 52		
n	104	110
Mean (SD)	0.51 (13.65)	-2.27 (15.88)
Week 52 (MMRM)		
n	106	111
LS mean (SE)	68.63 (1.89)	69.79 (1.85)
95% CI of LS mean	(64.91, 72.35)	(66.16, 73.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.16 (-4.05, 6.38)
Absolute Change at Week 52 (MMRM)		
n	103	110
LS mean (SE)	0.40 (1.46)	-2.17 (1.42)
95% CI of LS mean	(-2.49, 3.28)	(-4.96, 0.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.57 (-6.59, 1.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	106	114
LS mean (SE)	-1.00 (1.21)	-2.27 (1.17)
95% CI of LS mean	(-3.38, 1.38)	(-4.57, 0.03)
P-value within Treatment	0.4094	0.0531
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.27 (-4.59, 2.05)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4510
Hedges' G (SE)		-0.10 (0.13)
Hedges' 95% CI		(-0.37, 0.16)
Hedges' P-value		0.4503

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	80	73
Mean (SD)	65.42 (16.03)	65.87 (21.39)
Week 8 (MMRM)		
n	79	68
LS mean (SE)	62.94 (2.17)	65.62 (2.33)
95% CI of LS mean	(58.65, 67.23)	(61.02, 70.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.68 (-3.61, 8.98)
Absolute Change at Week 8 (MMRM)		
n	79	67
LS mean (SE)	-2.67 (2.06)	0.34 (2.22)
95% CI of LS mean	(-6.74, 1.39)	(-4.05, 4.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.02 (-2.97, 9.01)
Week 16 (MMRM)		
n	78	69
LS mean (SE)	62.56 (2.33)	64.93 (2.48)
95% CI of LS mean	(57.95, 67.17)	(60.03, 69.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.37 (-4.37, 9.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	78	68
LS mean (SE)	-3.02 (1.99)	0.34 (2.13)
95% CI of LS mean	(-6.96, 0.92)	(-3.88, 4.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.36 (-2.42, 9.14)
Week 24 (MMRM)		
n	78	68
LS mean (SE)	61.07 (2.40)	64.23 (2.56)
95% CI of LS mean	(56.32, 65.81)	(59.16, 69.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.16 (-3.79, 10.11)
Absolute Change at Week 24 (MMRM)		
n	78	67
LS mean (SE)	-4.52 (2.10)	-1.29 (2.26)
95% CI of LS mean	(-8.66, -0.37)	(-5.75, 3.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.22 (-2.87, 9.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	77	68
Mean (SD)	64.29 (18.23)	67.77 (19.42)
Absolute Change at Week 52		
n	77	66
Mean (SD)	-1.30 (16.39)	2.15 (21.20)
Week 52 (MMRM)		
n	76	64
LS mean (SE)	64.12 (2.12)	67.87 (2.29)
95% CI of LS mean	(59.93, 68.31)	(63.35, 72.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.75 (-2.42, 9.92)
Absolute Change at Week 52 (MMRM)		
n	76	63
LS mean (SE)	-1.53 (2.14)	2.37 (2.33)
95% CI of LS mean	(-5.77, 2.71)	(-2.25, 6.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.90 (-2.38, 10.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	78	68
LS mean (SE)	-3.02 (1.71)	0.47 (1.83)
95% CI of LS mean	(-6.40, 0.35)	(-3.16, 4.10)
P-value within Treatment	0.0788	0.7977
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.49 (-1.47, 8.45)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1660
Hedges' G (SE)		0.23 (0.17)
Hedges' 95% CI		(-0.10, 0.56)
Hedges' P-value		0.1668

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	83	84
Mean (SD)	67.57 (16.26)	68.75 (20.69)
Week 8 (MMRM)		
n	83	82
LS mean (SE)	65.32 (2.13)	65.80 (2.13)
95% CI of LS mean	(61.12, 69.52)	(61.59, 70.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.48 (-5.47, 6.43)
Absolute Change at Week 8 (MMRM)		
n	82	81
LS mean (SE)	-2.35 (1.80)	-3.08 (1.81)
95% CI of LS mean	(-5.91, 1.20)	(-6.65, 0.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.72 (-5.77, 4.32)
Week 16 (MMRM)		
n	83	83
LS mean (SE)	65.32 (2.26)	68.11 (2.26)
95% CI of LS mean	(60.86, 69.78)	(63.66, 72.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.80 (-3.52, 9.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	82	82
LS mean (SE)	-2.25 (1.70)	-0.69 (1.70)
95% CI of LS mean	(-5.60, 1.10)	(-4.04, 2.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.56 (-3.18, 6.30)
Week 24 (MMRM)		
n	83	82
LS mean (SE)	63.61 (2.26)	65.91 (2.26)
95% CI of LS mean	(59.15, 68.07)	(61.44, 70.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.30 (-4.02, 8.62)
Absolute Change at Week 24 (MMRM)		
n	82	81
LS mean (SE)	-3.98 (1.80)	-2.97 (1.81)
95% CI of LS mean	(-7.53, -0.43)	(-6.53, 0.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.01 (-4.02, 6.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	82	76
Mean (SD)	66.36 (17.74)	67.87 (21.29)
Absolute Change at Week 52		
n	81	75
Mean (SD)	-1.34 (14.76)	-0.33 (17.67)
Week 52 (MMRM)		
n	81	75
LS mean (SE)	66.28 (2.15)	68.45 (2.18)
95% CI of LS mean	(62.04, 70.52)	(64.14, 72.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.17 (-3.88, 8.23)
Absolute Change at Week 52 (MMRM)		
n	80	74
LS mean (SE)	-1.48 (1.82)	-0.42 (1.87)
95% CI of LS mean	(-5.08, 2.11)	(-4.11, 3.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.07 (-4.09, 6.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	82	82
LS mean (SE)	-2.57 (1.45)	-1.36 (1.46)
95% CI of LS mean	(-5.43, 0.29)	(-4.23, 1.51)
P-value within Treatment	0.0774	0.3514
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.21 (-2.85, 5.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5560
Hedges' G (SE)		0.09 (0.16)
Hedges' 95% CI		(-0.22, 0.40)
Hedges' P-value		0.5558

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	106	103
Mean (SD)	66.17 (18.82)	70.39 (19.62)
Week 8 (MMRM)		
n	106	101
LS mean (SE)	64.90 (1.89)	69.50 (1.93)
95% CI of LS mean	(61.18, 68.62)	(65.68, 73.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.60 (-0.74, 9.93)
Absolute Change at Week 8 (MMRM)		
n	104	100
LS mean (SE)	-1.85 (1.80)	-0.35 (1.84)
95% CI of LS mean	(-5.40, 1.70)	(-3.97, 3.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.50 (-3.57, 6.58)
Week 16 (MMRM)		
n	104	101
LS mean (SE)	64.13 (1.99)	67.39 (2.03)
95% CI of LS mean	(60.20, 68.06)	(63.39, 71.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.26 (-2.35, 8.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	102	100
LS mean (SE)	-2.31 (1.69)	-2.01 (1.71)
95% CI of LS mean	(-5.64, 1.02)	(-5.38, 1.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.30 (-4.44, 5.05)
Week 24 (MMRM)		
n	104	101
LS mean (SE)	64.93 (2.05)	68.80 (2.08)
95% CI of LS mean	(60.89, 68.96)	(64.70, 72.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.88 (-1.88, 9.64)
Absolute Change at Week 24 (MMRM)		
n	102	100
LS mean (SE)	-1.73 (1.70)	-1.17 (1.72)
95% CI of LS mean	(-5.08, 1.61)	(-4.55, 2.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.57 (-4.19, 5.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	102	103
Mean (SD)	67.32 (19.36)	69.74 (19.10)
Absolute Change at Week 52		
n	100	101
Mean (SD)	0.61 (14.96)	-0.83 (18.54)
Week 52 (MMRM)		
n	101	100
LS mean (SE)	67.22 (1.89)	69.46 (1.91)
95% CI of LS mean	(63.49, 70.94)	(65.69, 73.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.24 (-3.06, 7.54)
Absolute Change at Week 52 (MMRM)		
n	99	99
LS mean (SE)	0.54 (1.69)	-0.65 (1.70)
95% CI of LS mean	(-2.80, 3.88)	(-4.01, 2.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.18 (-5.92, 3.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	102	100
LS mean (SE)	-1.17 (1.38)	-1.27 (1.40)
95% CI of LS mean	(-3.89, 1.55)	(-4.03, 1.48)
P-value within Treatment	0.3981	0.3631
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-3.98, 3.77)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9578
Hedges' G (SE)		-0.01 (0.14)
Hedges' 95% CI		(-0.28, 0.27)
Hedges' P-value		0.9578

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	108	99
Mean (SD)	84.88 (26.72)	80.47 (30.49)
Week 8 (MMRM)		
n	109	98
LS mean (SE)	83.95 (2.53)	84.12 (2.67)
95% CI of LS mean	(78.96, 88.93)	(78.86, 89.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-7.09, 7.43)
Absolute Change at Week 8 (MMRM)		
n	107	96
LS mean (SE)	-1.25 (1.95)	3.80 (2.06)
95% CI of LS mean	(-5.10, 2.60)	(-0.27, 7.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.05 (-0.57, 10.66)
Week 16 (MMRM)		
n	109	98
LS mean (SE)	81.68 (2.78)	83.09 (2.93)
95% CI of LS mean	(76.20, 87.16)	(77.31, 88.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.41 (-6.57, 9.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	107	96
LS mean (SE)	-3.63 (2.32)	2.75 (2.45)
95% CI of LS mean	(-8.21, 0.96)	(-2.09, 7.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.38 (-0.30, 13.05)
Week 24 (MMRM)		
n	109	97
LS mean (SE)	86.37 (2.54)	83.58 (2.68)
95% CI of LS mean	(81.36, 91.37)	(78.29, 88.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.78 (-10.09, 4.52)
Absolute Change at Week 24 (MMRM)		
n	107	95
LS mean (SE)	1.38 (2.29)	3.19 (2.43)
95% CI of LS mean	(-3.15, 5.90)	(-1.60, 7.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.81 (-4.78, 8.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	108	94
Mean (SD)	86.73 (23.65)	81.56 (28.34)
Absolute Change at Week 52		
n	106	92
Mean (SD)	0.94 (22.75)	0.72 (21.53)
Week 52 (MMRM)		
n	108	93
LS mean (SE)	85.76 (2.52)	81.43 (2.69)
95% CI of LS mean	(80.78, 90.74)	(76.12, 86.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.34 (-11.63, 2.95)
Absolute Change at Week 52 (MMRM)		
n	106	91
LS mean (SE)	0.50 (2.11)	0.94 (2.26)
95% CI of LS mean	(-3.67, 4.66)	(-3.52, 5.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.44 (-5.67, 6.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	107	96
LS mean (SE)	-0.58 (1.87)	2.29 (1.98)
95% CI of LS mean	(-4.28, 3.11)	(-1.61, 6.20)
P-value within Treatment	0.7553	0.2484
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.88 (-2.51, 8.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2937
Hedges' G (SE)		0.15 (0.14)
Hedges' 95% CI		(-0.13, 0.42)
Hedges' P-value		0.2929

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	80	86
Mean (SD)	84.58 (27.53)	84.11 (27.40)
Week 8 (MMRM)		
n	79	85
LS mean (SE)	87.12 (3.01)	82.49 (2.90)
95% CI of LS mean	(81.18, 93.06)	(76.76, 88.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.63 (-12.89, 3.63)
Absolute Change at Week 8 (MMRM)		
n	78	85
LS mean (SE)	2.48 (2.50)	-1.49 (2.39)
95% CI of LS mean	(-2.45, 7.41)	(-6.22, 3.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.98 (-10.81, 2.86)
Week 16 (MMRM)		
n	78	86
LS mean (SE)	82.75 (3.23)	82.92 (3.09)
95% CI of LS mean	(76.37, 89.12)	(76.81, 89.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-8.67, 9.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	77	86
LS mean (SE)	-1.79 (2.72)	-1.10 (2.58)
95% CI of LS mean	(-7.15, 3.57)	(-6.19, 4.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.69 (-6.71, 8.09)
Week 24 (MMRM)		
n	78	85
LS mean (SE)	82.37 (3.51)	82.14 (3.37)
95% CI of LS mean	(75.43, 89.30)	(75.47, 88.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-9.85, 9.39)
Absolute Change at Week 24 (MMRM)		
n	77	85
LS mean (SE)	-2.25 (2.90)	-1.88 (2.77)
95% CI of LS mean	(-7.98, 3.49)	(-7.35, 3.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-7.57, 8.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	74	82
Mean (SD)	85.14 (26.54)	82.93 (26.32)
Absolute Change at Week 52		
n	73	82
Mean (SD)	1.37 (28.02)	-1.22 (22.50)
Week 52 (MMRM)		
n	73	82
LS mean (SE)	84.77 (3.09)	82.14 (2.95)
95% CI of LS mean	(78.67, 90.87)	(76.32, 87.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.63 (-11.06, 5.80)
Absolute Change at Week 52 (MMRM)		
n	72	82
LS mean (SE)	0.28 (2.93)	-1.95 (2.77)
95% CI of LS mean	(-5.51, 6.06)	(-7.43, 3.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.23 (-10.20, 5.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	77	86
LS mean (SE)	-1.25 (2.47)	-1.64 (2.35)
95% CI of LS mean	(-6.13, 3.62)	(-6.29, 3.00)
P-value within Treatment	0.6125	0.4852
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.39 (-7.13, 6.35)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9090
Hedges' G (SE)		-0.02 (0.16)
Hedges' 95% CI		(-0.33, 0.29)
Hedges' P-value		0.9089

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	21	20
Mean (SD)	73.02 (35.93)	71.67 (39.40)
Week 8 (MMRM)		
n	21	19
LS mean (SE)	76.06 (7.09)	75.59 (7.45)
95% CI of LS mean	(61.68, 90.43)	(60.47, 90.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-21.37, 20.43)
Absolute Change at Week 8 (MMRM)		
n	21	19
LS mean (SE)	2.59 (5.54)	5.91 (5.83)
95% CI of LS mean	(-8.64, 13.83)	(-5.91, 17.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.31 (-13.03, 19.66)
Week 16 (MMRM)		
n	20	19
LS mean (SE)	78.98 (6.51)	75.59 (6.76)
95% CI of LS mean	(65.81, 92.15)	(61.90, 89.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.39 (-22.44, 15.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	20	19
LS mean (SE)	5.93 (5.39)	5.91 (5.57)
95% CI of LS mean	(-5.01, 16.88)	(-5.41, 17.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-15.82, 15.77)
Week 24 (MMRM)		
n	20	19
LS mean (SE)	77.49 (7.39)	68.57 (7.69)
95% CI of LS mean	(62.50, 92.48)	(52.96, 84.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.92 (-30.61, 12.77)
Absolute Change at Week 24 (MMRM)		
n	20	19
LS mean (SE)	4.27 (5.70)	-1.11 (5.90)
95% CI of LS mean	(-7.28, 15.82)	(-13.08, 10.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.38 (-22.06, 11.30)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	18	20
Mean (SD)	79.63 (28.33)	81.67 (22.88)
Absolute Change at Week 52		
n	18	20
Mean (SD)	9.26 (40.91)	10.00 (28.82)
Week 52 (MMRM)		
n	18	19
LS mean (SE)	80.15 (5.96)	80.85 (5.98)
95% CI of LS mean	(68.07, 92.23)	(68.70, 93.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.70 (-16.48, 17.89)
Absolute Change at Week 52 (MMRM)		
n	18	19
LS mean (SE)	6.82 (7.81)	11.17 (7.87)
95% CI of LS mean	(-8.99, 22.63)	(-4.79, 27.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.35 (-18.16, 26.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	20	19
LS mean (SE)	5.67 (5.51)	5.32 (5.68)
95% CI of LS mean	(-5.49, 16.84)	(-6.19, 16.84)
P-value within Treatment	0.3098	0.3548
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.35 (-16.44, 15.74)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9648
Hedges' G (SE)		-0.01 (0.31)
Hedges' 95% CI		(-0.65, 0.62)
Hedges' P-value		0.9646

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	86.31 (25.36)	83.63 (27.35)
Week 8 (MMRM)		
n	167	164
LS mean (SE)	86.55 (2.01)	84.13 (2.03)
95% CI of LS mean	(82.60, 90.50)	(80.14, 88.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.43 (-8.04, 3.19)
Absolute Change at Week 8 (MMRM)		
n	164	162
LS mean (SE)	0.17 (1.60)	0.66 (1.61)
95% CI of LS mean	(-2.98, 3.33)	(-2.51, 3.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.49 (-3.99, 4.97)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	82.66 (2.23)	83.74 (2.25)
95% CI of LS mean	(78.27, 87.05)	(79.31, 88.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.08 (-5.16, 7.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	-3.84 (1.89)	0.25 (1.89)
95% CI of LS mean	(-7.55, -0.13)	(-3.48, 3.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.09 (-1.17, 9.35)
Week 24 (MMRM)		
n	167	163
LS mean (SE)	85.68 (2.17)	84.41 (2.19)
95% CI of LS mean	(81.41, 89.94)	(80.10, 88.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.27 (-7.33, 4.80)
Absolute Change at Week 24 (MMRM)		
n	164	161
LS mean (SE)	-0.59 (1.89)	0.92 (1.90)
95% CI of LS mean	(-4.30, 3.13)	(-2.82, 4.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.50 (-3.77, 6.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	86.87 (24.33)	82.60 (27.77)
Absolute Change at Week 52		
n	162	156
Mean (SD)	0.21 (22.44)	-1.50 (20.51)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	86.11 (2.08)	81.66 (2.11)
95% CI of LS mean	(82.03, 90.20)	(77.52, 85.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.45 (-10.27, 1.37)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	-0.29 (1.71)	-1.87 (1.73)
95% CI of LS mean	(-3.66, 3.08)	(-5.28, 1.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.58 (-6.37, 3.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	-1.57 (1.55)	-0.23 (1.56)
95% CI of LS mean	(-4.63, 1.48)	(-3.31, 2.84)
P-value within Treatment	0.3117	0.8807
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.34 (-3.00, 5.67)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5440
Hedges' G (SE)		0.07 (0.11)
Hedges' 95% CI		(-0.15, 0.28)
Hedges' P-value		0.5439

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	78.95 (33.72)	70.83 (36.26)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	81.65 (7.86)	73.87 (8.60)
95% CI of LS mean	(65.58, 97.72)	(56.29, 91.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.78 (-32.08, 16.51)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	2.66 (4.53)	3.09 (4.95)
95% CI of LS mean	(-6.59, 11.92)	(-7.03, 13.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-13.55, 14.41)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	78.15 (8.01)	78.04 (8.76)
95% CI of LS mean	(61.75, 94.54)	(60.11, 95.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-24.87, 24.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-0.85 (6.26)	7.26 (6.83)
95% CI of LS mean	(-13.63, 11.93)	(-6.69, 21.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.10 (-11.00, 27.21)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	85.16 (7.83)	78.04 (8.57)
95% CI of LS mean	(69.13, 101.19)	(60.51, 95.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.13 (-31.36, 17.11)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	6.17 (6.07)	7.26 (6.63)
95% CI of LS mean	(-6.21, 18.55)	(-6.26, 20.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.09 (-17.44, 19.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	81.48 (30.73)	73.81 (37.39)
Absolute Change at Week 52		
n	18	13
Mean (SD)	1.85 (33.28)	0.00 (13.61)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	79.79 (8.55)	67.52 (9.64)
95% CI of LS mean	(62.23, 97.35)	(47.79, 87.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-12.28 (-39.09, 14.54)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	0.84 (6.33)	-3.60 (7.27)
95% CI of LS mean	(-12.14, 13.81)	(-18.45, 11.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.44 (-24.31, 15.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	2.05 (5.15)	3.64 (5.68)
95% CI of LS mean	(-8.46, 12.56)	(-7.94, 15.21)
P-value within Treatment	0.6929	0.5264
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.58 (-14.27, 17.44)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8399
Hedges' G (SE)		0.07 (0.33)
Hedges' 95% CI		(-0.61, 0.74)
Hedges' P-value		0.8374

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	169	169
Mean (SD)	85.40 (26.18)	83.23 (28.20)
Week 8 (MMRM)		
n	169	167
LS mean (SE)	85.77 (1.99)	84.17 (2.01)
95% CI of LS mean	(81.84, 89.69)	(80.23, 88.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.59 (-7.16, 3.98)
Absolute Change at Week 8 (MMRM)		
n	166	165
LS mean (SE)	0.17 (1.66)	1.04 (1.67)
95% CI of LS mean	(-3.09, 3.44)	(-2.24, 4.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.87 (-3.76, 5.50)
Week 16 (MMRM)		
n	168	168
LS mean (SE)	82.69 (2.17)	83.39 (2.17)
95% CI of LS mean	(78.42, 86.95)	(79.12, 87.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.70 (-5.33, 6.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	165	166
LS mean (SE)	-2.98 (1.84)	0.23 (1.84)
95% CI of LS mean	(-6.61, 0.64)	(-3.39, 3.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.22 (-1.91, 8.34)
Week 24 (MMRM)		
n	168	166
LS mean (SE)	84.68 (2.17)	83.24 (2.18)
95% CI of LS mean	(80.41, 88.95)	(78.95, 87.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.44 (-7.49, 4.62)
Absolute Change at Week 24 (MMRM)		
n	165	164
LS mean (SE)	-0.76 (1.90)	0.06 (1.90)
95% CI of LS mean	(-4.49, 2.97)	(-3.67, 3.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.83 (-4.45, 6.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	164	164
Mean (SD)	86.59 (24.13)	83.13 (26.24)
Absolute Change at Week 52		
n	161	162
Mean (SD)	1.04 (23.99)	-0.21 (22.44)
Week 52 (MMRM)		
n	163	162
LS mean (SE)	86.06 (1.98)	82.85 (1.98)
95% CI of LS mean	(82.18, 89.95)	(78.95, 86.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.21 (-8.72, 2.30)
Absolute Change at Week 52 (MMRM)		
n	160	160
LS mean (SE)	0.46 (1.83)	-0.33 (1.83)
95% CI of LS mean	(-3.15, 4.07)	(-3.94, 3.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.79 (-5.90, 4.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	165	166
LS mean (SE)	-1.10 (1.59)	-0.01 (1.59)
95% CI of LS mean	(-4.22, 2.03)	(-3.14, 3.11)
P-value within Treatment	0.4909	0.9941
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.08 (-3.34, 5.51)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6301
Hedges' G (SE)		0.05 (0.11)
Hedges' 95% CI		(-0.16, 0.27)
Hedges' P-value		0.6299

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	109	114
Mean (SD)	83.18 (27.45)	77.19 (32.38)
Week 8 (MMRM)		
n	109	115
LS mean (SE)	82.16 (2.82)	78.65 (2.76)
95% CI of LS mean	(76.61, 87.71)	(73.21, 84.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.52 (-11.30, 4.26)
Absolute Change at Week 8 (MMRM)		
n	106	114
LS mean (SE)	-1.32 (2.29)	1.27 (2.22)
95% CI of LS mean	(-5.83, 3.19)	(-3.10, 5.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.59 (-3.71, 8.88)
Week 16 (MMRM)		
n	109	115
LS mean (SE)	78.64 (3.05)	77.20 (2.98)
95% CI of LS mean	(72.64, 84.65)	(71.33, 83.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.45 (-9.86, 6.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	106	114
LS mean (SE)	-5.00 (2.49)	-0.19 (2.41)
95% CI of LS mean	(-9.91, -0.10)	(-4.94, 4.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.81 (-2.03, 11.65)
Week 24 (MMRM)		
n	109	114
LS mean (SE)	80.78 (3.02)	78.45 (2.95)
95% CI of LS mean	(74.84, 86.73)	(72.62, 84.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.34 (-10.67, 6.00)
Absolute Change at Week 24 (MMRM)		
n	106	113
LS mean (SE)	-2.48 (2.39)	1.04 (2.32)
95% CI of LS mean	(-7.20, 2.23)	(-3.53, 5.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.53 (-3.05, 10.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	107	111
Mean (SD)	81.93 (28.33)	78.98 (29.79)
Absolute Change at Week 52		
n	104	110
Mean (SD)	-1.92 (23.14)	0.61 (23.02)
Week 52 (MMRM)		
n	106	111
LS mean (SE)	80.78 (2.87)	77.59 (2.81)
95% CI of LS mean	(75.13, 86.43)	(72.06, 83.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.19 (-11.11, 4.73)
Absolute Change at Week 52 (MMRM)		
n	103	110
LS mean (SE)	-2.75 (2.29)	0.12 (2.21)
95% CI of LS mean	(-7.26, 1.75)	(-4.25, 4.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.87 (-3.41, 9.15)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	106	114
LS mean (SE)	-3.41 (2.04)	0.32 (1.97)
95% CI of LS mean	(-7.43, 0.60)	(-3.57, 4.21)
P-value within Treatment	0.0952	0.8709
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.73 (-1.87, 9.34)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1901
Hedges' G (SE)		0.18 (0.13)
Hedges' 95% CI		(-0.09, 0.44)
Hedges' P-value		0.1901

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	80	73
Mean (SD)	87.08 (26.25)	90.41 (20.40)
Week 8 (MMRM)		
n	79	68
LS mean (SE)	89.97 (2.27)	90.78 (2.43)
95% CI of LS mean	(85.49, 94.46)	(85.98, 95.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.81 (-5.76, 7.39)
Absolute Change at Week 8 (MMRM)		
n	79	67
LS mean (SE)	3.09 (1.88)	0.82 (2.02)
95% CI of LS mean	(-0.62, 6.79)	(-3.19, 4.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.27 (-7.73, 3.19)
Week 16 (MMRM)		
n	78	69
LS mean (SE)	87.33 (2.42)	92.24 (2.57)
95% CI of LS mean	(82.55, 92.11)	(87.16, 97.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.92 (-2.07, 11.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	78	68
LS mean (SE)	0.55 (2.45)	2.28 (2.62)
95% CI of LS mean	(-4.29, 5.39)	(-2.91, 7.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.73 (-5.37, 8.83)
Week 24 (MMRM)		
n	78	68
LS mean (SE)	90.31 (2.52)	89.79 (2.69)
95% CI of LS mean	(85.32, 95.30)	(84.46, 95.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.52 (-7.82, 6.78)
Absolute Change at Week 24 (MMRM)		
n	78	67
LS mean (SE)	3.53 (2.73)	-0.19 (2.94)
95% CI of LS mean	(-1.87, 8.93)	(-6.00, 5.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.72 (-11.66, 4.21)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	76	68
Mean (SD)	92.11 (17.10)	88.24 (21.37)
Absolute Change at Week 52		
n	76	66
Mean (SD)	5.26 (26.70)	-1.52 (19.77)
Week 52 (MMRM)		
n	75	64
LS mean (SE)	91.94 (2.20)	87.89 (2.37)
95% CI of LS mean	(87.59, 96.29)	(83.20, 92.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.05 (-10.46, 2.35)
Absolute Change at Week 52 (MMRM)		
n	75	63
LS mean (SE)	5.29 (2.68)	-1.84 (2.90)
95% CI of LS mean	(-0.01, 10.58)	(-7.58, 3.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.13 (-14.94, 0.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	78	68
LS mean (SE)	3.12 (2.22)	0.08 (2.38)
95% CI of LS mean	(-1.26, 7.51)	(-4.63, 4.79)
P-value within Treatment	0.1613	0.9729
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.04 (-9.48, 3.40)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3519
Hedges' G (SE)		-0.15 (0.17)
Hedges' 95% CI		(-0.48, 0.17)
Hedges' P-value		0.3522

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	83	84
Mean (SD)	86.35 (26.05)	82.94 (27.62)
Week 8 (MMRM)		
n	83	82
LS mean (SE)	87.36 (3.08)	82.05 (3.09)
95% CI of LS mean	(81.28, 93.44)	(75.96, 88.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.32 (-13.93, 3.30)
Absolute Change at Week 8 (MMRM)		
n	82	81
LS mean (SE)	1.19 (2.12)	-0.81 (2.12)
95% CI of LS mean	(-2.99, 5.37)	(-5.00, 3.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.00 (-7.93, 3.92)
Week 16 (MMRM)		
n	83	83
LS mean (SE)	83.35 (3.10)	85.73 (3.10)
95% CI of LS mean	(77.22, 89.48)	(79.60, 91.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-6.30, 11.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	82	82
LS mean (SE)	-2.87 (2.67)	2.87 (2.67)
95% CI of LS mean	(-8.15, 2.41)	(-2.41, 8.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.74 (-1.73, 13.22)
Week 24 (MMRM)		
n	83	81
LS mean (SE)	85.76 (3.32)	83.01 (3.34)
95% CI of LS mean	(79.19, 92.32)	(76.42, 89.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.75 (-12.06, 6.57)
Absolute Change at Week 24 (MMRM)		
n	82	80
LS mean (SE)	-0.43 (2.63)	0.11 (2.65)
95% CI of LS mean	(-5.62, 4.76)	(-5.12, 5.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.54 (-6.83, 7.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	82	76
Mean (SD)	86.99 (25.53)	83.33 (27.49)
Absolute Change at Week 52		
n	81	75
Mean (SD)	0.82 (21.07)	-0.44 (20.86)
Week 52 (MMRM)		
n	81	75
LS mean (SE)	86.92 (2.99)	81.72 (3.04)
95% CI of LS mean	(81.01, 92.84)	(75.73, 87.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.20 (-13.63, 3.23)
Absolute Change at Week 52 (MMRM)		
n	80	74
LS mean (SE)	0.80 (2.37)	-1.25 (2.42)
95% CI of LS mean	(-3.88, 5.48)	(-6.04, 3.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.05 (-8.74, 4.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	82	82
LS mean (SE)	-0.84 (2.17)	0.58 (2.18)
95% CI of LS mean	(-5.13, 3.46)	(-3.73, 4.89)
P-value within Treatment	0.7011	0.7920
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.41 (-4.67, 7.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6475
Hedges' G (SE)		0.07 (0.16)
Hedges' 95% CI		(-0.24, 0.38)
Hedges' P-value		0.6473

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	106	103
Mean (SD)	83.65 (27.70)	81.88 (30.17)
Week 8 (MMRM)		
n	105	101
LS mean (SE)	83.94 (2.48)	84.10 (2.54)
95% CI of LS mean	(79.04, 88.84)	(79.09, 89.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-6.85, 7.17)
Absolute Change at Week 8 (MMRM)		
n	103	100
LS mean (SE)	-0.06 (2.22)	2.72 (2.26)
95% CI of LS mean	(-4.44, 4.32)	(-1.73, 7.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.78 (-3.47, 9.03)
Week 16 (MMRM)		
n	104	101
LS mean (SE)	81.53 (2.84)	80.45 (2.90)
95% CI of LS mean	(75.92, 87.13)	(74.73, 86.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.08 (-9.09, 6.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	102	100
LS mean (SE)	-2.52 (2.40)	-0.96 (2.43)
95% CI of LS mean	(-7.26, 2.22)	(-5.76, 3.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.56 (-5.19, 8.30)
Week 24 (MMRM)		
n	104	101
LS mean (SE)	84.13 (2.67)	82.41 (2.72)
95% CI of LS mean	(78.85, 89.40)	(77.04, 87.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.71 (-9.24, 5.82)
Absolute Change at Week 24 (MMRM)		
n	102	100
LS mean (SE)	0.41 (2.50)	1.04 (2.53)
95% CI of LS mean	(-4.52, 5.34)	(-3.95, 6.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-6.38, 7.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	101	103
Mean (SD)	85.48 (24.23)	81.88 (27.13)
Absolute Change at Week 52		
n	99	101
Mean (SD)	1.35 (27.73)	0.00 (22.61)
Week 52 (MMRM)		
n	100	100
LS mean (SE)	84.45 (2.56)	81.38 (2.59)
95% CI of LS mean	(79.39, 89.51)	(76.27, 86.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.07 (-10.27, 4.12)
Absolute Change at Week 52 (MMRM)		
n	98	99
LS mean (SE)	0.41 (2.52)	0.03 (2.53)
95% CI of LS mean	(-4.57, 5.39)	(-4.97, 5.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-7.44, 6.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	102	100
LS mean (SE)	-0.57 (2.12)	0.04 (2.14)
95% CI of LS mean	(-4.74, 3.61)	(-4.19, 4.26)
P-value within Treatment	0.7895	0.9864
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.60 (-5.34, 6.54)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8418
Hedges' G (SE)		0.03 (0.14)
Hedges' 95% CI		(-0.25, 0.30)
Hedges' P-value		0.8417

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-102.sas Creation: 17DEC2024 14:17

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA	VNZ/TEZ/D-IVA
	N = 4	N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
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- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
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- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-cg-52wks-sub-102.sas Creation: 17DEC2024 14:18

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-abs-cfqr-nonrd-cg-52wks-sub-102.sas Creation: 17DEC2024 14:18

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
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- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.6364
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.4824
Region (North America vs. Rest of the World) [1]	0.8582

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.12.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.6968
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.2381
Region (North America vs. Rest of the World) [1]	0.1158

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.12.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.2214
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.7160
Region (North America vs. Rest of the World) [1]	0.7554

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.12.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.0939
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.7154
Region (North America vs. Rest of the World) [1]	0.1247

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 5
Baseline		
n	9	5
Mean (SD)	80.86 (12.14)	74.44 (42.05)
Week 52		
n	8	5
Mean (SD)	82.64 (10.04)	86.67 (11.52)
Absolute Change at Week 52		
n	8	5
Mean (SD)	0.69 (8.63)	12.22 (44.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 5
Absolute Change at Week 52 (MMRM)		
n	8	5
LS mean (SE)	1.73 (10.26)	10.56 (13.03)
95% CI of LS mean	(-21.49, 24.95)	(-18.92, 40.04)
P-value within Treatment	0.8696	0.4387
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.82 (-28.99, 46.64)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6103
Hedges' G (SE)		0.28 (0.53)
Hedges' 95% CI		(-0.89, 1.46)
Hedges' P-value		0.6069

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	19
Mean (SD)	80.56 (15.78)	79.82 (24.51)
Week 52		
n	20	18
Mean (SD)	83.06 (18.86)	83.64 (16.66)
Absolute Change at Week 52		
n	20	17
Mean (SD)	2.78 (23.05)	5.88 (25.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	17
LS mean (SE)	3.05 (5.58)	5.56 (6.06)
95% CI of LS mean	(-8.31, 14.41)	(-6.77, 17.89)
P-value within Treatment	0.5884	0.3655
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.51 (-14.34, 19.36)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7637
Hedges' G (SE)		0.10 (0.32)
Hedges' 95% CI		(-0.56, 0.75)
Hedges' P-value		0.7626

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Age at screening ≥18 years

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 27	VNZ/TEZ/D-IVA N = 25

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Male

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 11
Baseline		
n	19	11
Mean (SD)	79.24 (16.44)	73.74 (37.28)
Week 52		
n	18	10
Mean (SD)	82.72 (18.07)	85.56 (14.39)
Absolute Change at Week 52		
n	18	10
Mean (SD)	2.78 (22.08)	14.44 (40.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Male

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 52 (MMRM)		
n	18	10
LS mean (SE)	3.33 (7.23)	13.45 (9.73)
95% CI of LS mean	(-11.59, 18.25)	(-6.63, 33.53)
P-value within Treatment	0.6491	0.1796
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.12 (-15.02, 35.26)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4144
Hedges' G (SE)		0.32 (0.39)
Hedges' 95% CI		(-0.47, 1.11)
Hedges' P-value		0.4139

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Female

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	14
Mean (SD)	82.87 (11.47)	84.13 (17.28)
Week 52		
n	10	14
Mean (SD)	83.33 (14.58)	84.52 (16.76)
Absolute Change at Week 52		
n	10	13
Mean (SD)	1.11 (16.10)	1.28 (15.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Female

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	10	12
LS mean (SE)	3.09 (5.37)	-0.26 (4.86)
95% CI of LS mean	(-8.19, 14.37)	(-10.48, 9.96)
P-value within Treatment	0.5721	0.9580
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.35 (-19.18, 12.48)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6621
Hedges' G (SE)		-0.19 (0.41)
Hedges' 95% CI		(-1.05, 0.67)
Hedges' P-value		0.6494

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = North America

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 10
Baseline		
n	15	10
Mean (SD)	80.74 (15.69)	73.89 (28.93)
Week 52		
n	14	10
Mean (SD)	83.33 (12.52)	78.89 (18.11)
Absolute Change at Week 52		
n	14	10
Mean (SD)	1.59 (13.15)	5.00 (31.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = North America

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 52 (MMRM)		
n	14	10
LS mean (SE)	0.67 (6.51)	6.28 (7.83)
95% CI of LS mean	(-12.90, 14.24)	(-10.05, 22.61)
P-value within Treatment	0.9185	0.4319
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.61 (-16.63, 27.85)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6048
Hedges' G (SE)		0.22 (0.40)
Hedges' 95% CI		(-0.61, 1.05)
Hedges' P-value		0.5874

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = Rest of World

	ELX/TEZ/IVA N = 16	VNZ/TEZ/D-IVA N = 16
Baseline		
n	16	15
Mean (SD)	80.56 (14.05)	83.33 (27.22)
Week 52		
n	14	14
Mean (SD)	82.54 (20.42)	89.29 (12.22)
Absolute Change at Week 52		
n	14	13
Mean (SD)	2.78 (25.39)	8.55 (28.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = Rest of World

	ELX/TEZ/IVA N = 16	VNZ/TEZ/D-IVA N = 16
Absolute Change at Week 52 (MMRM)		
n	14	12
LS mean (SE)	2.58 (7.65)	9.49 (8.27)
95% CI of LS mean	(-13.28, 18.45)	(-7.67, 26.64)
P-value within Treatment	0.7389	0.2638
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.90 (-16.61, 30.41)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5487
Hedges' G (SE)		0.23 (0.38)
Hedges' 95% CI		(-0.56, 1.02)
Hedges' P-value		0.5472

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 5
Baseline		
n	9	5
Mean (SD)	93.06 (18.60)	100.00 (0.00)
Week 52		
n	8	5
Mean (SD)	96.09 (8.80)	100.00 (0.00)
Absolute Change at Week 52		
n	8	5
Mean (SD)	3.91 (11.05)	0.00 (0.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 5
Absolute Change at Week 52 (MMRM)		
n	8	5
LS mean (SE)	3.96 (2.74)	-0.08 (3.48)
95% CI of LS mean	(-2.24, 10.15)	(-7.95, 7.78)
P-value within Treatment	0.1822	0.9813
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.04 (-14.13, 6.05)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3884
Hedges' G (SE)		-0.48 (0.54)
Hedges' 95% CI		(-1.67, 0.70)
Hedges' P-value		0.3875

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	18
Mean (SD)	97.44 (10.68)	98.26 (4.70)
Week 52		
n	20	18
Mean (SD)	97.19 (8.72)	93.75 (15.01)
Absolute Change at Week 52		
n	20	16
Mean (SD)	-2.50 (8.93)	-3.52 (12.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-tsqm-abs-wk52-sub-102.sas Creation: 17DEC2024 14:06

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	16
LS mean (SE)	-2.69 (2.35)	-3.28 (2.63)
95% CI of LS mean	(-7.48, 2.10)	(-8.64, 2.08)
P-value within Treatment	0.2617	0.2213
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.60 (-7.83, 6.63)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8676
Hedges' G (SE)		-0.06 (0.33)
Hedges' 95% CI		(-0.72, 0.61)
Hedges' P-value		0.8668

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Age at screening ≥18 years

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 27	VNZ/TEZ/D-IVA N = 25

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Male

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 11
Baseline		
n	19	11
Mean (SD)	97.04 (12.90)	100.00 (0.00)
Week 52		
n	18	10
Mean (SD)	97.22 (8.08)	96.25 (11.86)
Absolute Change at Week 52		
n	18	10
Mean (SD)	0.35 (9.70)	-3.75 (11.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Male

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 52 (MMRM)		
n	18	10
LS mean (SE)	0.57 (2.47)	-4.15 (3.32)
95% CI of LS mean	(-4.53, 5.66)	(-11.00, 2.71)
P-value within Treatment	0.8201	0.2239
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.71 (-13.29, 3.87)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2681
Hedges' G (SE)		-0.44 (0.39)
Hedges' 95% CI		(-1.23, 0.36)
Hedges' P-value		0.2699

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Female

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	13
Mean (SD)	94.79 (14.31)	97.60 (5.44)
Week 52		
n	10	14
Mean (SD)	96.25 (9.86)	94.64 (14.47)
Absolute Change at Week 52		
n	10	12
Mean (SD)	-2.50 (10.29)	-1.56 (9.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Female

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	10	11
LS mean (SE)	-3.50 (3.47)	-0.79 (3.29)
95% CI of LS mean	(-10.82, 3.81)	(-7.73, 6.15)
P-value within Treatment	0.3263	0.8126
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.71 (-7.84, 13.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5949
Hedges' G (SE)		0.24 (0.42)
Hedges' 95% CI		(-0.64, 1.12)
Hedges' P-value		0.5784

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = North America

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 10
Baseline		
n	15	9
Mean (SD)	96.25 (14.52)	97.92 (6.25)
Week 52		
n	14	10
Mean (SD)	95.98 (10.29)	91.25 (18.68)
Absolute Change at Week 52		
n	14	9
Mean (SD)	0.00 (12.26)	-7.64 (15.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = North America

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 52 (MMRM)		
n	14	9
LS mean (SE)	0.61 (3.55)	-8.58 (4.56)
95% CI of LS mean	(-6.83, 8.04)	(-18.13, 0.97)
P-value within Treatment	0.8666	0.0754
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.19 (-22.03, 3.66)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1510
Hedges' G (SE)		-0.66 (0.42)
Hedges' 95% CI		(-1.54, 0.22)
Hedges' P-value		0.1346

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-tsqm-abs-wk52-sub-102.sas Creation: 17DEC2024 14:06

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = Rest of World

	ELX/TEZ/IVA N = 16	VNZ/TEZ/D-IVA N = 16
Baseline		
n	16	15
Mean (SD)	96.09 (12.47)	99.17 (2.20)
Week 52		
n	14	14
Mean (SD)	97.77 (6.76)	98.21 (6.68)
Absolute Change at Week 52		
n	14	13
Mean (SD)	-1.34 (7.01)	0.96 (2.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = Rest of World

	ELX/TEZ/IVA N = 16	VNZ/TEZ/D-IVA N = 16
Absolute Change at Week 52 (MMRM)		
n	14	12
LS mean (SE)	-1.13 (1.46)	0.79 (1.57)
95% CI of LS mean	(-4.15, 1.89)	(-2.47, 4.06)
P-value within Treatment	0.4472	0.6191
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.92 (-2.55, 6.39)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3830
Hedges' G (SE)		0.34 (0.38)
Hedges' 95% CI		(-0.45, 1.13)
Hedges' P-value		0.3829

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-tsqm-abs-wk52-sub-102.sas Creation: 17DEC2024 14:06

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 5
Baseline		
n	9	5
Mean (SD)	74.69 (15.49)	83.33 (10.39)
Week 52		
n	8	5
Mean (SD)	87.50 (18.96)	84.44 (10.69)
Absolute Change at Week 52		
n	8	5
Mean (SD)	11.81 (17.68)	1.11 (16.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 5
Absolute Change at Week 52 (MMRM)		
n	8	5
LS mean (SE)	11.34 (5.51)	1.86 (6.99)
95% CI of LS mean	(-1.12, 23.80)	(-13.96, 17.67)
P-value within Treatment	0.0696	0.7967
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.49 (-29.77, 10.80)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3178
Hedges' G (SE)		-0.57 (0.54)
Hedges' 95% CI		(-1.76, 0.63)
Hedges' P-value		0.3188

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	19
Mean (SD)	80.30 (14.52)	82.16 (16.73)
Week 52		
n	20	18
Mean (SD)	80.28 (23.12)	85.80 (13.64)
Absolute Change at Week 52		
n	20	17
Mean (SD)	0.28 (17.70)	4.25 (15.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	17
LS mean (SE)	0.04 (3.71)	4.53 (4.03)
95% CI of LS mean	(-7.51, 7.59)	(-3.67, 12.73)
P-value within Treatment	0.9914	0.2694
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.49 (-6.72, 15.69)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4210
Hedges' G (SE)		0.26 (0.32)
Hedges' 95% CI		(-0.39, 0.92)
Hedges' P-value		0.4205

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Age at screening ≥18 years

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 27	VNZ/TEZ/D-IVA N = 25

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Male

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 11
Baseline		
n	19	11
Mean (SD)	78.95 (13.30)	82.83 (13.71)
Week 52		
n	18	10
Mean (SD)	82.10 (23.92)	86.67 (9.87)
Absolute Change at Week 52		
n	18	10
Mean (SD)	2.47 (20.54)	5.00 (12.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Male

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 52 (MMRM)		
n	18	10
LS mean (SE)	2.94 (4.30)	4.15 (5.79)
95% CI of LS mean	(-5.94, 11.82)	(-7.80, 16.10)
P-value within Treatment	0.5007	0.4802
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.21 (-13.75, 16.17)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8687
Hedges' G (SE)		0.06 (0.38)
Hedges' 95% CI		(-0.72, 0.85)
Hedges' P-value		0.8679

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Female

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	14
Mean (SD)	78.24 (17.48)	83.33 (17.30)
Week 52		
n	10	14
Mean (SD)	82.78 (18.97)	85.71 (15.05)
Absolute Change at Week 52		
n	10	13
Mean (SD)	5.56 (13.61)	2.14 (17.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Female

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	10	12
LS mean (SE)	6.09 (5.56)	1.87 (5.04)
95% CI of LS mean	(-5.59, 17.77)	(-8.71, 12.45)
P-value within Treatment	0.2877	0.7150
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.22 (-20.62, 12.17)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5951
Hedges' G (SE)		-0.23 (0.41)
Hedges' 95% CI		(-1.09, 0.63)
Hedges' P-value		0.5808

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = North America

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 10
Baseline		
n	15	10
Mean (SD)	78.15 (16.33)	82.78 (15.81)
Week 52		
n	14	10
Mean (SD)	83.73 (19.91)	85.00 (14.12)
Absolute Change at Week 52		
n	14	10
Mean (SD)	4.76 (15.69)	2.22 (14.15)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = North America

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 52 (MMRM)		
n	14	10
LS mean (SE)	3.90 (3.95)	3.43 (4.76)
95% CI of LS mean	(-4.35, 12.15)	(-6.50, 13.35)
P-value within Treatment	0.3359	0.4793
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-13.99, 13.05)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9430
Hedges' G (SE)		-0.03 (0.40)
Hedges' 95% CI		(-0.86, 0.80)
Hedges' P-value		0.9400

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = Rest of World

	ELX/TEZ/IVA N = 16	VNZ/TEZ/D-IVA N = 16
Baseline		
n	16	15
Mean (SD)	79.17 (13.68)	83.33 (15.85)
Week 52		
n	14	14
Mean (SD)	80.95 (24.43)	86.90 (12.44)
Absolute Change at Week 52		
n	14	13
Mean (SD)	2.38 (20.87)	4.27 (16.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = Rest of World

	ELX/TEZ/IVA N = 16	VNZ/TEZ/D-IVA N = 16
Absolute Change at Week 52 (MMRM)		
n	14	12
LS mean (SE)	2.49 (5.39)	4.50 (5.83)
95% CI of LS mean	(-8.69, 13.67)	(-7.58, 16.59)
P-value within Treatment	0.6487	0.4478
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.01 (-14.55, 18.58)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8032
Hedges' G (SE)		0.10 (0.38)
Hedges' 95% CI		(-0.69, 0.88)
Hedges' P-value		0.8019

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 5
Baseline		
n	9	5
Mean (SD)	76.19 (7.14)	92.86 (7.14)
Week 52		
n	8	5
Mean (SD)	88.39 (11.41)	85.71 (11.29)
Absolute Change at Week 52		
n	8	5
Mean (SD)	11.61 (10.06)	-7.14 (13.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 5
Absolute Change at Week 52 (MMRM)		
n	8	5
LS mean (SE)	10.62 (3.14)	-5.56 (3.99)
95% CI of LS mean	(3.51, 17.73)	(-14.59, 3.47)
P-value within Treatment	0.0082	0.1969
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-16.18 (-27.77, -4.60)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0115
Hedges' G (SE)		-1.69 (0.63)
Hedges' 95% CI		(-3.07, -0.31)
Hedges' P-value		0.0205

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	19
Mean (SD)	84.09 (18.03)	84.21 (16.07)
Week 52		
n	20	18
Mean (SD)	86.79 (17.54)	86.51 (15.86)
Absolute Change at Week 52		
n	20	17
Mean (SD)	2.86 (14.17)	3.78 (18.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	17
LS mean (SE)	3.37 (3.67)	3.18 (3.99)
95% CI of LS mean	(-4.10, 10.84)	(-4.93, 11.29)
P-value within Treatment	0.3654	0.4307
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.19 (-11.27, 10.89)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9724
Hedges' G (SE)		-0.01 (0.32)
Hedges' 95% CI		(-0.67, 0.64)
Hedges' P-value		0.9722

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Age at screening ≥18 years

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 27	VNZ/TEZ/D-IVA N = 25

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Male

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 11
Baseline		
n	19	11
Mean (SD)	80.45 (18.11)	88.31 (14.02)
Week 52		
n	18	10
Mean (SD)	88.10 (14.49)	88.57 (13.13)
Absolute Change at Week 52		
n	18	10
Mean (SD)	7.14 (11.75)	0.71 (20.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Male

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 52 (MMRM)		
n	18	10
LS mean (SE)	6.93 (3.57)	1.09 (4.81)
95% CI of LS mean	(-0.44, 14.31)	(-8.83, 11.01)
P-value within Treatment	0.0641	0.8222
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.84 (-18.26, 6.58)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3415
Hedges' G (SE)		-0.37 (0.39)
Hedges' 95% CI		(-1.17, 0.42)
Hedges' P-value		0.3420

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Female

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	14
Mean (SD)	83.93 (12.23)	85.20 (15.96)
Week 52		
n	10	14
Mean (SD)	85.71 (18.75)	85.71 (16.09)
Absolute Change at Week 52		
n	10	13
Mean (SD)	2.14 (16.51)	1.65 (16.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Female

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	10	12
LS mean (SE)	3.17 (5.65)	0.93 (5.12)
95% CI of LS mean	(-8.70, 15.05)	(-9.83, 11.69)
P-value within Treatment	0.5817	0.8581
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.24 (-18.91, 14.43)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7807
Hedges' G (SE)		-0.12 (0.41)
Hedges' 95% CI		(-0.98, 0.74)
Hedges' P-value		0.7719

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = North America

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 10
Baseline		
n	15	10
Mean (SD)	76.67 (16.08)	83.57 (15.81)
Week 52		
n	14	10
Mean (SD)	84.69 (16.54)	82.14 (16.92)
Absolute Change at Week 52		
n	14	10
Mean (SD)	7.65 (8.62)	-1.43 (18.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = North America

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 52 (MMRM)		
n	14	10
LS mean (SE)	7.37 (3.82)	-1.03 (4.60)
95% CI of LS mean	(-0.61, 15.34)	(-10.62, 8.57)
P-value within Treatment	0.0683	0.8258
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.39 (-21.46, 4.68)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1955
Hedges' G (SE)		-0.56 (0.41)
Hedges' 95% CI		(-1.41, 0.28)
Hedges' P-value		0.1817

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = Rest of World

	ELX/TEZ/IVA N = 16	VNZ/TEZ/D-IVA N = 16
Baseline		
n	16	15
Mean (SD)	86.61 (14.73)	88.57 (14.49)
Week 52		
n	14	14
Mean (SD)	89.80 (15.27)	90.31 (12.41)
Absolute Change at Week 52		
n	14	13
Mean (SD)	3.06 (17.21)	3.30 (17.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = Rest of World

	ELX/TEZ/IVA N = 16	VNZ/TEZ/D-IVA N = 16
Absolute Change at Week 52 (MMRM)		
n	14	12
LS mean (SE)	2.00 (4.36)	4.81 (4.71)
95% CI of LS mean	(-7.04, 11.04)	(-4.96, 14.58)
P-value within Treatment	0.6509	0.3182
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.81 (-10.58, 16.20)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6674
Hedges' G (SE)		0.17 (0.38)
Hedges' 95% CI		(-0.62, 0.95)
Hedges' P-value		0.6657

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\t-qs-mmrm-tsqm-abs-wk52-sub-102.sas Creation: 17DEC2024 14:06

Table 1.2.2.13.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.9104
Age at screening (<18 years vs. ≥18 years) [2]	0.8744
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.7878
Sex (Male vs. Female) [1]	0.4517
Region (North America vs. Rest of the World) [1]	0.2500

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.13.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Physical Activity

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.5108
Age at screening (<18 years vs. ≥18 years) [2]	0.4426
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.0276
Sex (Male vs. Female) [1]	0.4745
Region (North America vs. Rest of the World) [1]	0.0714

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.13.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Social Activity

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.7627
Age at screening (<18 years vs. ≥18 years) [2]	0.2478
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.6487
Sex (Male vs. Female) [1]	0.3895
Region (North America vs. Rest of the World) [1]	0.4780

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.13.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Emotional

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.9860
Age at screening (<18 years vs. ≥18 years) [2]	0.7849
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.4578
Sex (Male vs. Female) [1]	0.8848
Region (North America vs. Rest of the World) [1]	0.7084

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.13.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Work/School Limitation

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1487
Age at screening (<18 years vs. ≥18 years) [2]	0.6490
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.1302
Sex (Male vs. Female) [1]	0.2959
Region (North America vs. Rest of the World) [1]	0.7776

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	109	99
Mean (SD)	10.77 (4.39)	10.74 (4.12)
Week 4 (MMRM)		
n	109	98
LS mean (SE)	10.30 (0.37)	10.33 (0.39)
95% CI of LS mean	(9.58, 11.03)	(9.56, 11.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.03 (-1.04, 1.09)
Absolute Change at Week 4 (MMRM)		
n	104	96
LS mean (SE)	-0.38 (0.24)	-0.26 (0.25)
95% CI of LS mean	(-0.85, 0.08)	(-0.74, 0.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-0.55, 0.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 24 (MMRM)		
n	112	94
LS mean (SE)	10.79 (0.40)	10.91 (0.43)
95% CI of LS mean	(9.99, 11.58)	(10.06, 11.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-1.04, 1.29)
Absolute Change at Week 24 (MMRM)		
n	108	92
LS mean (SE)	0.08 (0.29)	0.33 (0.31)
95% CI of LS mean	(-0.50, 0.65)	(-0.29, 0.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.25 (-0.60, 1.10)
Week 52		
n	111	93
Mean (SD)	10.44 (4.14)	10.51 (4.19)
Absolute Change at Week 52		
n	106	91
Mean (SD)	-0.26 (2.96)	-0.24 (3.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52 (MMRM)		
n	111	92
LS mean (SE)	10.47 (0.39)	10.55 (0.43)
95% CI of LS mean	(9.69, 11.24)	(9.71, 11.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-1.06, 1.23)
Absolute Change at Week 52 (MMRM)		
n	106	90
LS mean (SE)	-0.26 (0.31)	-0.08 (0.33)
95% CI of LS mean	(-0.88, 0.35)	(-0.74, 0.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-0.72, 1.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	108	94
LS mean (SE)	-0.09 (0.26)	0.12 (0.28)
95% CI of LS mean	(-0.61, 0.42)	(-0.43, 0.68)
P-value within Treatment	0.7206	0.6582
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.22 (-0.54, 0.97)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5714
Hedges' G (SE)		0.08 (0.14)
Hedges' 95% CI		(-0.20, 0.36)
Hedges' P-value		0.5706

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	86	89
Mean (SD)	9.90 (2.95)	9.80 (3.30)
Week 4 (MMRM)		
n	82	92
LS mean (SE)	9.77 (0.36)	9.83 (0.34)
95% CI of LS mean	(9.06, 10.48)	(9.15, 10.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.06 (-0.93, 1.04)
Absolute Change at Week 4 (MMRM)		
n	81	89
LS mean (SE)	-0.12 (0.23)	-0.02 (0.22)
95% CI of LS mean	(-0.58, 0.34)	(-0.46, 0.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-0.54, 0.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 24 (MMRM)		
n	81	84
LS mean (SE)	9.91 (0.39)	9.69 (0.38)
95% CI of LS mean	(9.14, 10.68)	(8.94, 10.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-1.30, 0.85)
Absolute Change at Week 24 (MMRM)		
n	80	82
LS mean (SE)	0.07 (0.30)	-0.10 (0.30)
95% CI of LS mean	(-0.53, 0.66)	(-0.69, 0.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-1.00, 0.67)
Week 52		
n	76	86
Mean (SD)	9.50 (3.17)	9.76 (3.04)
Absolute Change at Week 52		
n	75	83
Mean (SD)	-0.59 (2.55)	-0.20 (2.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52 (MMRM)		
n	75	86
LS mean (SE)	9.38 (0.35)	9.74 (0.33)
95% CI of LS mean	(8.70, 10.07)	(9.09, 10.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-0.58, 1.31)
Absolute Change at Week 52 (MMRM)		
n	74	83
LS mean (SE)	-0.54 (0.31)	-0.13 (0.30)
95% CI of LS mean	(-1.16, 0.08)	(-0.73, 0.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.41 (-0.45, 1.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	81	86
LS mean (SE)	-0.24 (0.27)	-0.12 (0.26)
95% CI of LS mean	(-0.77, 0.30)	(-0.64, 0.40)
P-value within Treatment	0.3894	0.6574
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-0.63, 0.87)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7562
Hedges' G (SE)		0.05 (0.15)
Hedges' 95% CI		(-0.26, 0.35)
Hedges' P-value		0.7561

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	30	25
Mean (SD)	10.23 (2.87)	9.24 (3.22)
Week 4 (MMRM)		
n	29	25
LS mean (SE)	9.74 (0.48)	9.40 (0.52)
95% CI of LS mean	(8.78, 10.70)	(8.36, 10.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.34 (-1.76, 1.08)
Absolute Change at Week 4 (MMRM)		
n	28	24
LS mean (SE)	-0.42 (0.47)	-0.08 (0.51)
95% CI of LS mean	(-1.37, 0.52)	(-1.11, 0.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.34 (-1.06, 1.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 24 (MMRM)		
n	28	23
LS mean (SE)	10.25 (0.59)	9.45 (0.65)
95% CI of LS mean	(9.08, 11.43)	(8.15, 10.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.81 (-2.57, 0.95)
Absolute Change at Week 24 (MMRM)		
n	27	22
LS mean (SE)	0.15 (0.55)	0.08 (0.60)
95% CI of LS mean	(-0.95, 1.24)	(-1.13, 1.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-1.71, 1.58)
Week 52		
n	27	24
Mean (SD)	9.78 (3.36)	8.83 (2.78)
Absolute Change at Week 52		
n	26	23
Mean (SD)	-0.38 (3.24)	-0.48 (2.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52 (MMRM)		
n	27	23
LS mean (SE)	9.75 (0.61)	9.00 (0.66)
95% CI of LS mean	(8.54, 10.97)	(7.67, 10.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.76 (-2.56, 1.04)
Absolute Change at Week 52 (MMRM)		
n	26	22
LS mean (SE)	-0.39 (0.61)	-0.43 (0.66)
95% CI of LS mean	(-1.61, 0.83)	(-1.76, 0.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-1.85, 1.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	27	23
LS mean (SE)	-0.12 (0.50)	-0.17 (0.54)
95% CI of LS mean	(-1.12, 0.88)	(-1.27, 0.92)
P-value within Treatment	0.8053	0.7522
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-1.54, 1.44)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9470
Hedges' G (SE)		-0.02 (0.28)
Hedges' 95% CI		(-0.58, 0.54)
Hedges' P-value		0.9468

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	166	166
Mean (SD)	10.42 (3.99)	10.38 (3.84)
Week 4 (MMRM)		
n	162	165
LS mean (SE)	10.11 (0.29)	10.22 (0.29)
95% CI of LS mean	(9.54, 10.69)	(9.65, 10.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.11 (-0.70, 0.92)
Absolute Change at Week 4 (MMRM)		
n	157	161
LS mean (SE)	-0.23 (0.18)	-0.15 (0.18)
95% CI of LS mean	(-0.58, 0.13)	(-0.50, 0.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-0.42, 0.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 24 (MMRM)		
n	165	155
LS mean (SE)	10.42 (0.32)	10.49 (0.32)
95% CI of LS mean	(9.80, 11.04)	(9.86, 11.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-0.82, 0.96)
Absolute Change at Week 24 (MMRM)		
n	161	152
LS mean (SE)	0.07 (0.23)	0.13 (0.23)
95% CI of LS mean	(-0.38, 0.51)	(-0.33, 0.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.06 (-0.58, 0.70)
Week 52		
n	161	157
Mean (SD)	10.10 (3.86)	10.31 (3.78)
Absolute Change at Week 52		
n	156	153
Mean (SD)	-0.42 (2.73)	-0.18 (3.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52 (MMRM)		
n	159	155
LS mean (SE)	10.03 (0.30)	10.36 (0.30)
95% CI of LS mean	(9.45, 10.61)	(9.77, 10.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.33 (-0.49, 1.16)
Absolute Change at Week 52 (MMRM)		
n	154	151
LS mean (SE)	-0.36 (0.24)	-0.06 (0.24)
95% CI of LS mean	(-0.83, 0.11)	(-0.53, 0.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.30 (-0.36, 0.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	162	157
LS mean (SE)	-0.15 (0.20)	0.03 (0.21)
95% CI of LS mean	(-0.55, 0.25)	(-0.37, 0.44)
P-value within Treatment	0.4668	0.8691
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-0.39, 0.75)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5299
Hedges' G (SE)		0.07 (0.11)
Hedges' 95% CI		(-0.15, 0.29)
Hedges' P-value		0.5299

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	17	17
Mean (SD)	10.29 (2.87)	11.12 (4.66)
Week 4 (MMRM)		
n	18	16
LS mean (SE)	10.56 (0.85)	11.05 (0.92)
95% CI of LS mean	(8.82, 12.30)	(9.17, 12.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.49 (-2.13, 3.11)
Absolute Change at Week 4 (MMRM)		
n	16	16
LS mean (SE)	0.15 (0.66)	-0.48 (0.67)
95% CI of LS mean	(-1.20, 1.50)	(-1.84, 0.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.63 (-2.57, 1.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 24 (MMRM)		
n	18	15
LS mean (SE)	10.81 (0.93)	11.14 (1.02)
95% CI of LS mean	(8.89, 12.72)	(9.05, 13.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.34 (-2.54, 3.21)
Absolute Change at Week 24 (MMRM)		
n	17	15
LS mean (SE)	0.33 (0.76)	-0.31 (0.80)
95% CI of LS mean	(-1.22, 1.88)	(-1.94, 1.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-2.91, 1.63)
Week 52		
n	17	13
Mean (SD)	10.59 (3.76)	12.31 (4.66)
Absolute Change at Week 52		
n	15	13
Mean (SD)	-0.53 (2.07)	0.08 (3.04)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52 (MMRM)		
n	17	13
LS mean (SE)	10.37 (0.99)	12.33 (1.12)
95% CI of LS mean	(8.33, 12.40)	(10.04, 14.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.97 (-1.13, 5.07)
Absolute Change at Week 52 (MMRM)		
n	15	13
LS mean (SE)	-0.27 (0.65)	-0.19 (0.69)
95% CI of LS mean	(-1.61, 1.07)	(-1.62, 1.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-1.90, 2.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	17	16
LS mean (SE)	0.03 (0.46)	-0.25 (0.49)
95% CI of LS mean	(-0.92, 0.98)	(-1.25, 0.76)
P-value within Treatment	0.9455	0.6158
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.28 (-1.69, 1.13)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6861
Hedges' G (SE)		-0.14 (0.34)
Hedges' 95% CI		(-0.84, 0.55)
Hedges' P-value		0.6794

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	178	172
Mean (SD)	10.39 (3.93)	10.12 (3.69)
Week 4 (MMRM)		
n	173	174
LS mean (SE)	10.00 (0.27)	10.03 (0.27)
95% CI of LS mean	(9.46, 10.53)	(9.49, 10.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.03 (-0.72, 0.79)
Absolute Change at Week 4 (MMRM)		
n	169	169
LS mean (SE)	-0.28 (0.17)	-0.13 (0.17)
95% CI of LS mean	(-0.62, 0.05)	(-0.47, 0.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-0.33, 0.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 24 (MMRM)		
n	175	163
LS mean (SE)	10.34 (0.30)	10.28 (0.30)
95% CI of LS mean	(9.75, 10.92)	(9.68, 10.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-0.89, 0.77)
Absolute Change at Week 24 (MMRM)		
n	171	159
LS mean (SE)	0.07 (0.22)	0.14 (0.23)
95% CI of LS mean	(-0.36, 0.50)	(-0.30, 0.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-0.55, 0.69)
Week 52		
n	170	167
Mean (SD)	9.96 (3.78)	9.91 (3.55)
Absolute Change at Week 52		
n	166	162
Mean (SD)	-0.43 (2.84)	-0.24 (3.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52 (MMRM)		
n	169	165
LS mean (SE)	9.94 (0.28)	10.01 (0.28)
95% CI of LS mean	(9.39, 10.49)	(9.45, 10.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-0.71, 0.85)
Absolute Change at Week 52 (MMRM)		
n	165	160
LS mean (SE)	-0.35 (0.23)	-0.16 (0.24)
95% CI of LS mean	(-0.81, 0.11)	(-0.63, 0.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-0.47, 0.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	172	164
LS mean (SE)	-0.14 (0.20)	-0.01 (0.20)
95% CI of LS mean	(-0.53, 0.26)	(-0.41, 0.39)
P-value within Treatment	0.4902	0.9509
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-0.44, 0.69)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6610
Hedges' G (SE)		0.05 (0.11)
Hedges' 95% CI		(-0.17, 0.26)
Hedges' P-value		0.6609

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	115	114
Mean (SD)	10.03 (3.68)	9.71 (3.46)
Week 4 (MMRM)		
n	112	115
LS mean (SE)	9.65 (0.32)	9.75 (0.32)
95% CI of LS mean	(9.02, 10.28)	(9.12, 10.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-0.79, 0.99)
Absolute Change at Week 4 (MMRM)		
n	108	113
LS mean (SE)	-0.24 (0.20)	0.07 (0.19)
95% CI of LS mean	(-0.63, 0.14)	(-0.31, 0.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.31 (-0.23, 0.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 24 (MMRM)		
n	115	108
LS mean (SE)	10.00 (0.34)	9.75 (0.34)
95% CI of LS mean	(9.34, 10.67)	(9.08, 10.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-1.20, 0.69)
Absolute Change at Week 24 (MMRM)		
n	111	106
LS mean (SE)	0.11 (0.25)	0.10 (0.25)
95% CI of LS mean	(-0.38, 0.61)	(-0.40, 0.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.01 (-0.71, 0.69)
Week 52		
n	112	110
Mean (SD)	9.70 (3.46)	10.03 (3.90)
Absolute Change at Week 52		
n	108	108
Mean (SD)	-0.28 (2.31)	0.17 (2.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52 (MMRM)		
n	111	110
LS mean (SE)	9.76 (0.34)	9.96 (0.34)
95% CI of LS mean	(9.08, 10.43)	(9.28, 10.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.20 (-0.76, 1.16)
Absolute Change at Week 52 (MMRM)		
n	107	108
LS mean (SE)	-0.16 (0.25)	0.23 (0.25)
95% CI of LS mean	(-0.66, 0.34)	(-0.27, 0.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.39 (-0.32, 1.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	112
LS mean (SE)	-0.02 (0.22)	0.17 (0.22)
95% CI of LS mean	(-0.46, 0.42)	(-0.27, 0.60)
P-value within Treatment	0.9193	0.4594
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.19 (-0.44, 0.81)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5532
Hedges' G (SE)		0.08 (0.13)
Hedges' 95% CI		(-0.18, 0.34)
Hedges' P-value		0.5522

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	81	77
Mean (SD)	10.90 (4.01)	11.00 (4.11)
Week 4 (MMRM)		
n	79	75
LS mean (SE)	10.60 (0.43)	10.71 (0.45)
95% CI of LS mean	(9.75, 11.45)	(9.83, 11.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.11 (-1.12, 1.33)
Absolute Change at Week 4 (MMRM)		
n	77	72
LS mean (SE)	-0.29 (0.29)	-0.47 (0.31)
95% CI of LS mean	(-0.87, 0.29)	(-1.08, 0.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-1.02, 0.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 24 (MMRM)		
n	78	70
LS mean (SE)	10.92 (0.49)	11.31 (0.51)
95% CI of LS mean	(9.95, 11.89)	(10.29, 12.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.39 (-1.02, 1.80)
Absolute Change at Week 24 (MMRM)		
n	77	68
LS mean (SE)	0.02 (0.37)	0.16 (0.39)
95% CI of LS mean	(-0.71, 0.75)	(-0.61, 0.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-0.92, 1.20)
Week 52		
n	76	71
Mean (SD)	10.58 (4.20)	10.24 (3.36)
Absolute Change at Week 52		
n	74	68
Mean (SD)	-0.61 (3.39)	-0.82 (3.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52 (MMRM)		
n	75	68
LS mean (SE)	10.30 (0.43)	10.51 (0.45)
95% CI of LS mean	(9.45, 11.15)	(9.62, 11.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.21 (-1.02, 1.45)
Absolute Change at Week 52 (MMRM)		
n	73	65
LS mean (SE)	-0.68 (0.40)	-0.66 (0.43)
95% CI of LS mean	(-1.47, 0.12)	(-1.50, 0.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.02 (-1.14, 1.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	78	68
LS mean (SE)	-0.33 (0.33)	-0.25 (0.35)
95% CI of LS mean	(-0.98, 0.32)	(-0.94, 0.44)
P-value within Treatment	0.3199	0.4788
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-0.87, 1.03)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8675
Hedges' G (SE)		0.03 (0.17)
Hedges' 95% CI		(-0.30, 0.35)
Hedges' P-value		0.8674

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	9.85 (3.61)	10.16 (3.25)
Week 4 (MMRM)		
n	85	84
LS mean (SE)	9.97 (0.38)	9.80 (0.38)
95% CI of LS mean	(9.22, 10.71)	(9.04, 10.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-1.23, 0.89)
Absolute Change at Week 4 (MMRM)		
n	82	82
LS mean (SE)	0.05 (0.25)	-0.30 (0.26)
95% CI of LS mean	(-0.45, 0.56)	(-0.80, 0.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.35 (-1.06, 0.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 24 (MMRM)		
n	88	82
LS mean (SE)	10.07 (0.43)	10.44 (0.44)
95% CI of LS mean	(9.22, 10.92)	(9.57, 11.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.37 (-0.85, 1.59)
Absolute Change at Week 24 (MMRM)		
n	86	80
LS mean (SE)	0.14 (0.29)	0.40 (0.30)
95% CI of LS mean	(-0.44, 0.71)	(-0.19, 1.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.27 (-0.56, 1.10)
Week 52		
n	85	78
Mean (SD)	9.92 (3.67)	10.01 (3.75)
Absolute Change at Week 52		
n	82	76
Mean (SD)	-0.20 (2.83)	-0.24 (2.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52 (MMRM)		
n	84	77
LS mean (SE)	9.73 (0.40)	10.06 (0.41)
95% CI of LS mean	(8.95, 10.52)	(9.25, 10.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.32 (-0.80, 1.45)
Absolute Change at Week 52 (MMRM)		
n	81	75
LS mean (SE)	-0.24 (0.31)	-0.12 (0.32)
95% CI of LS mean	(-0.85, 0.37)	(-0.75, 0.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-0.76, 1.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	86	80
LS mean (SE)	-0.05 (0.25)	0.14 (0.26)
95% CI of LS mean	(-0.55, 0.44)	(-0.37, 0.65)
P-value within Treatment	0.8345	0.5811
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.20 (-0.52, 0.91)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5884
Hedges' G (SE)		0.08 (0.15)
Hedges' 95% CI		(-0.22, 0.39)
Hedges' P-value		0.5883

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	108	106
Mean (SD)	10.83 (3.97)	10.28 (4.17)
Week 4 (MMRM)		
n	106	106
LS mean (SE)	10.12 (0.36)	10.37 (0.36)
95% CI of LS mean	(9.41, 10.82)	(9.66, 11.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.25 (-0.75, 1.26)
Absolute Change at Week 4 (MMRM)		
n	103	103
LS mean (SE)	-0.50 (0.22)	-0.02 (0.22)
95% CI of LS mean	(-0.94, -0.07)	(-0.46, 0.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.48 (-0.14, 1.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 24 (MMRM)		
n	105	96
LS mean (SE)	10.66 (0.38)	10.27 (0.39)
95% CI of LS mean	(9.91, 11.40)	(9.51, 11.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-1.45, 0.68)
Absolute Change at Week 24 (MMRM)		
n	102	94
LS mean (SE)	0.03 (0.30)	-0.11 (0.31)
95% CI of LS mean	(-0.56, 0.61)	(-0.71, 0.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-0.98, 0.70)
Week 52		
n	103	103
Mean (SD)	10.17 (3.89)	10.18 (3.66)
Absolute Change at Week 52		
n	100	100
Mean (SD)	-0.59 (2.76)	-0.20 (3.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52 (MMRM)		
n	102	101
LS mean (SE)	10.20 (0.36)	10.28 (0.37)
95% CI of LS mean	(9.48, 10.92)	(9.56, 11.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-0.94, 1.10)
Absolute Change at Week 52 (MMRM)		
n	99	98
LS mean (SE)	-0.46 (0.31)	-0.11 (0.32)
95% CI of LS mean	(-1.08, 0.16)	(-0.74, 0.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.35 (-0.53, 1.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	103	100
LS mean (SE)	-0.22 (0.27)	-0.11 (0.28)
95% CI of LS mean	(-0.75, 0.32)	(-0.66, 0.44)
P-value within Treatment	0.4292	0.6929
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.11 (-0.66, 0.87)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7849
Hedges' G (SE)		0.04 (0.14)
Hedges' 95% CI		(-0.24, 0.31)
Hedges' P-value		0.7849

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	109	99
Mean (SD)	12.32 (4.65)	12.53 (4.82)
Week 4 (MMRM)		
n	108	98
LS mean (SE)	11.85 (0.41)	11.86 (0.43)
95% CI of LS mean	(11.05, 12.66)	(11.01, 12.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-1.16, 1.19)
Absolute Change at Week 4 (MMRM)		
n	103	96
LS mean (SE)	-0.34 (0.35)	-0.48 (0.36)
95% CI of LS mean	(-1.02, 0.34)	(-1.19, 0.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-1.13, 0.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 24 (MMRM)		
n	112	94
LS mean (SE)	12.30 (0.47)	12.34 (0.51)
95% CI of LS mean	(11.36, 13.23)	(11.33, 13.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.04 (-1.34, 1.42)
Absolute Change at Week 24 (MMRM)		
n	108	92
LS mean (SE)	0.11 (0.36)	-0.08 (0.39)
95% CI of LS mean	(-0.60, 0.82)	(-0.85, 0.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.19 (-1.24, 0.86)
Week 52		
n	111	93
Mean (SD)	11.95 (4.51)	11.78 (4.23)
Absolute Change at Week 52		
n	106	91
Mean (SD)	-0.15 (3.39)	-0.82 (4.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52 (MMRM)		
n	111	92
LS mean (SE)	12.04 (0.41)	11.72 (0.44)
95% CI of LS mean	(11.23, 12.84)	(10.85, 12.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.32 (-1.51, 0.87)
Absolute Change at Week 52 (MMRM)		
n	106	90
LS mean (SE)	-0.15 (0.37)	-0.72 (0.40)
95% CI of LS mean	(-0.87, 0.58)	(-1.50, 0.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.57 (-1.64, 0.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	108	94
LS mean (SE)	-0.02 (0.31)	-0.40 (0.33)
95% CI of LS mean	(-0.63, 0.59)	(-1.05, 0.26)
P-value within Treatment	0.9498	0.2313
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-1.27, 0.52)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4052
Hedges' G (SE)		-0.12 (0.14)
Hedges' 95% CI		(-0.39, 0.16)
Hedges' P-value		0.4042

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	86	88
Mean (SD)	10.36 (3.29)	10.24 (3.67)
Week 4 (MMRM)		
n	82	91
LS mean (SE)	11.13 (0.42)	10.37 (0.40)
95% CI of LS mean	(10.29, 11.96)	(9.58, 11.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.76 (-1.91, 0.39)
Absolute Change at Week 4 (MMRM)		
n	81	87
LS mean (SE)	0.74 (0.28)	0.01 (0.28)
95% CI of LS mean	(0.18, 1.31)	(-0.53, 0.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.73 (-1.51, 0.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 24 (MMRM)		
n	81	84
LS mean (SE)	11.25 (0.43)	10.30 (0.42)
95% CI of LS mean	(10.40, 12.10)	(9.48, 11.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.95 (-2.13, 0.24)
Absolute Change at Week 24 (MMRM)		
n	80	82
LS mean (SE)	0.89 (0.32)	0.06 (0.32)
95% CI of LS mean	(0.25, 1.53)	(-0.57, 0.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.82 (-1.72, 0.08)
Week 52		
n	76	86
Mean (SD)	11.05 (3.69)	10.74 (3.83)
Absolute Change at Week 52		
n	75	82
Mean (SD)	0.52 (3.06)	0.37 (3.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52 (MMRM)		
n	75	86
LS mean (SE)	10.96 (0.43)	10.72 (0.40)
95% CI of LS mean	(10.12, 11.80)	(9.93, 11.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-1.39, 0.92)
Absolute Change at Week 52 (MMRM)		
n	74	82
LS mean (SE)	0.48 (0.37)	0.40 (0.36)
95% CI of LS mean	(-0.26, 1.22)	(-0.31, 1.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-1.10, 0.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	81	85
LS mean (SE)	0.68 (0.27)	0.23 (0.27)
95% CI of LS mean	(0.14, 1.23)	(-0.29, 0.76)
P-value within Treatment	0.0139	0.3864
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.45 (-1.21, 0.30)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2388
Hedges' G (SE)		-0.18 (0.15)
Hedges' 95% CI		(-0.49, 0.12)
Hedges' P-value		0.2392

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	30	25
Mean (SD)	10.73 (2.60)	10.20 (3.42)
Week 4 (MMRM)		
n	29	25
LS mean (SE)	10.26 (0.62)	10.61 (0.67)
95% CI of LS mean	(9.01, 11.51)	(9.26, 11.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.35 (-1.50, 2.20)
Absolute Change at Week 4 (MMRM)		
n	28	24
LS mean (SE)	-0.39 (0.43)	-0.16 (0.46)
95% CI of LS mean	(-1.24, 0.47)	(-1.08, 0.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.23 (-1.04, 1.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 24 (MMRM)		
n	28	23
LS mean (SE)	10.90 (0.65)	10.72 (0.71)
95% CI of LS mean	(9.60, 12.20)	(9.29, 12.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-2.12, 1.77)
Absolute Change at Week 24 (MMRM)		
n	27	22
LS mean (SE)	0.23 (0.56)	0.37 (0.61)
95% CI of LS mean	(-0.88, 1.35)	(-0.87, 1.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-1.53, 1.80)
Week 52		
n	27	24
Mean (SD)	10.96 (4.36)	10.21 (4.06)
Absolute Change at Week 52		
n	26	23
Mean (SD)	0.46 (3.58)	0.04 (3.52)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52 (MMRM)		
n	27	23
LS mean (SE)	10.99 (0.81)	10.57 (0.88)
95% CI of LS mean	(9.37, 12.62)	(8.81, 12.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.43 (-2.83, 1.98)
Absolute Change at Week 52 (MMRM)		
n	26	22
LS mean (SE)	0.45 (0.69)	0.23 (0.75)
95% CI of LS mean	(-0.94, 1.84)	(-1.28, 1.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-2.27, 1.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	27	23
LS mean (SE)	0.34 (0.48)	0.30 (0.53)
95% CI of LS mean	(-0.63, 1.31)	(-0.76, 1.36)
P-value within Treatment	0.4815	0.5747
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-1.48, 1.39)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9512
Hedges' G (SE)		-0.02 (0.28)
Hedges' 95% CI		(-0.58, 0.54)
Hedges' P-value		0.9511

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	166	165
Mean (SD)	11.58 (4.42)	11.61 (4.55)
Week 4 (MMRM)		
n	161	164
LS mean (SE)	11.71 (0.33)	11.29 (0.33)
95% CI of LS mean	(11.07, 12.36)	(10.65, 11.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.43 (-1.33, 0.48)
Absolute Change at Week 4 (MMRM)		
n	156	159
LS mean (SE)	0.23 (0.26)	-0.26 (0.26)
95% CI of LS mean	(-0.28, 0.74)	(-0.77, 0.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.50 (-1.21, 0.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 24 (MMRM)		
n	165	155
LS mean (SE)	11.96 (0.36)	11.53 (0.37)
95% CI of LS mean	(11.24, 12.67)	(10.80, 12.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.43 (-1.45, 0.60)
Absolute Change at Week 24 (MMRM)		
n	161	152
LS mean (SE)	0.48 (0.27)	-0.05 (0.28)
95% CI of LS mean	(-0.06, 1.01)	(-0.61, 0.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.53 (-1.30, 0.24)
Week 52		
n	161	157
Mean (SD)	11.70 (4.18)	11.38 (4.08)
Absolute Change at Week 52		
n	156	152
Mean (SD)	0.08 (3.21)	-0.34 (3.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52 (MMRM)		
n	159	155
LS mean (SE)	11.62 (0.32)	11.41 (0.32)
95% CI of LS mean	(10.99, 12.24)	(10.78, 12.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.21 (-1.09, 0.68)
Absolute Change at Week 52 (MMRM)		
n	154	150
LS mean (SE)	0.09 (0.29)	-0.25 (0.29)
95% CI of LS mean	(-0.48, 0.65)	(-0.82, 0.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.34 (-1.13, 0.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	162	156
LS mean (SE)	0.28 (0.23)	-0.15 (0.24)
95% CI of LS mean	(-0.17, 0.74)	(-0.62, 0.31)
P-value within Treatment	0.2247	0.5173
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.43 (-1.08, 0.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1896
Hedges' G (SE)		-0.15 (0.11)
Hedges' 95% CI		(-0.37, 0.07)
Hedges' P-value		0.1900

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	17	17
Mean (SD)	10.24 (3.01)	13.82 (7.09)
Week 4 (MMRM)		
n	18	16
LS mean (SE)	11.75 (1.00)	12.18 (1.08)
95% CI of LS mean	(9.71, 13.80)	(9.97, 14.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-2.61, 3.46)
Absolute Change at Week 4 (MMRM)		
n	16	16
LS mean (SE)	0.87 (1.25)	-1.57 (1.26)
95% CI of LS mean	(-1.69, 3.43)	(-4.16, 1.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.45 (-6.11, 1.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 24 (MMRM)		
n	18	15
LS mean (SE)	12.29 (1.13)	13.36 (1.24)
95% CI of LS mean	(9.96, 14.62)	(10.82, 15.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.07 (-2.41, 4.56)
Absolute Change at Week 24 (MMRM)		
n	17	15
LS mean (SE)	1.48 (0.72)	-0.35 (0.76)
95% CI of LS mean	(0.01, 2.96)	(-1.91, 1.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.83 (-4.02, 0.36)
Week 52		
n	17	13
Mean (SD)	10.65 (3.87)	12.92 (4.87)
Absolute Change at Week 52		
n	15	13
Mean (SD)	0.33 (3.48)	-2.15 (6.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52 (MMRM)		
n	17	13
LS mean (SE)	10.61 (1.02)	12.38 (1.15)
95% CI of LS mean	(8.53, 12.70)	(10.02, 14.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.76 (-1.41, 4.94)
Absolute Change at Week 52 (MMRM)		
n	15	13
LS mean (SE)	0.31 (1.30)	-1.93 (1.39)
95% CI of LS mean	(-2.36, 2.97)	(-4.80, 0.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.24 (-6.18, 1.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	17	16
LS mean (SE)	0.89 (0.79)	-1.14 (0.84)
95% CI of LS mean	(-0.74, 2.53)	(-2.87, 0.59)
P-value within Treatment	0.2686	0.1873
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.04 (-4.46, 0.39)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0957
Hedges' G (SE)		-0.60 (0.35)
Hedges' 95% CI		(-1.31, 0.11)
Hedges' P-value		0.0944

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	178	171
Mean (SD)	11.58 (4.29)	11.16 (4.03)
Week 4 (MMRM)		
n	172	173
LS mean (SE)	11.48 (0.31)	11.11 (0.31)
95% CI of LS mean	(10.88, 12.08)	(10.50, 11.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.37 (-1.22, 0.48)
Absolute Change at Week 4 (MMRM)		
n	168	167
LS mean (SE)	0.06 (0.22)	-0.11 (0.22)
95% CI of LS mean	(-0.38, 0.50)	(-0.55, 0.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-0.79, 0.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 24 (MMRM)		
n	175	163
LS mean (SE)	11.75 (0.34)	11.24 (0.35)
95% CI of LS mean	(11.08, 12.42)	(10.55, 11.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.51 (-1.47, 0.45)
Absolute Change at Week 24 (MMRM)		
n	171	159
LS mean (SE)	0.33 (0.26)	0.03 (0.27)
95% CI of LS mean	(-0.19, 0.84)	(-0.50, 0.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-1.04, 0.44)
Week 52		
n	170	167
Mean (SD)	11.66 (4.23)	11.05 (3.98)
Absolute Change at Week 52		
n	166	161
Mean (SD)	0.08 (3.24)	-0.15 (3.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52 (MMRM)		
n	169	165
LS mean (SE)	11.60 (0.31)	11.19 (0.31)
95% CI of LS mean	(11.00, 12.21)	(10.58, 11.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.41 (-1.27, 0.46)
Absolute Change at Week 52 (MMRM)		
n	165	159
LS mean (SE)	0.12 (0.26)	-0.04 (0.27)
95% CI of LS mean	(-0.40, 0.64)	(-0.57, 0.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.16 (-0.90, 0.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	172	163
LS mean (SE)	0.22 (0.22)	-0.01 (0.22)
95% CI of LS mean	(-0.20, 0.65)	(-0.44, 0.43)
P-value within Treatment	0.3028	0.9807
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-0.84, 0.38)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4613
Hedges' G (SE)		-0.08 (0.11)
Hedges' 95% CI		(-0.30, 0.13)
Hedges' P-value		0.4614

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	115	113
Mean (SD)	11.26 (4.47)	11.07 (4.07)
Week 4 (MMRM)		
n	111	114
LS mean (SE)	10.90 (0.37)	10.76 (0.36)
95% CI of LS mean	(10.18, 11.62)	(10.04, 11.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-1.16, 0.88)
Absolute Change at Week 4 (MMRM)		
n	107	111
LS mean (SE)	-0.14 (0.29)	-0.28 (0.29)
95% CI of LS mean	(-0.72, 0.43)	(-0.84, 0.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-0.94, 0.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 24 (MMRM)		
n	115	108
LS mean (SE)	11.50 (0.39)	10.82 (0.39)
95% CI of LS mean	(10.74, 12.27)	(10.04, 11.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.68 (-1.78, 0.41)
Absolute Change at Week 24 (MMRM)		
n	111	106
LS mean (SE)	0.39 (0.30)	-0.26 (0.30)
95% CI of LS mean	(-0.19, 0.98)	(-0.86, 0.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.66 (-1.50, 0.19)
Week 52		
n	112	110
Mean (SD)	11.22 (4.01)	11.35 (4.07)
Absolute Change at Week 52		
n	108	107
Mean (SD)	0.03 (2.76)	0.10 (3.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52 (MMRM)		
n	111	110
LS mean (SE)	11.21 (0.37)	11.30 (0.37)
95% CI of LS mean	(10.48, 11.94)	(10.56, 12.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-0.96, 1.12)
Absolute Change at Week 52 (MMRM)		
n	107	107
LS mean (SE)	0.07 (0.28)	0.13 (0.28)
95% CI of LS mean	(-0.49, 0.63)	(-0.43, 0.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.06 (-0.74, 0.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	111
LS mean (SE)	0.23 (0.25)	-0.07 (0.25)
95% CI of LS mean	(-0.25, 0.72)	(-0.56, 0.42)
P-value within Treatment	0.3481	0.7843
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-0.99, 0.39)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3938
Hedges' G (SE)		-0.11 (0.13)
Hedges' 95% CI		(-0.38, 0.15)
Hedges' P-value		0.3925

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	81	77
Mean (SD)	11.73 (3.78)	11.94 (4.90)
Week 4 (MMRM)		
n	79	75
LS mean (SE)	12.27 (0.47)	11.92 (0.49)
95% CI of LS mean	(11.34, 13.20)	(10.96, 12.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.35 (-1.69, 1.00)
Absolute Change at Week 4 (MMRM)		
n	77	72
LS mean (SE)	0.54 (0.38)	-0.21 (0.39)
95% CI of LS mean	(-0.20, 1.29)	(-0.98, 0.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.75 (-1.82, 0.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 24 (MMRM)		
n	78	70
LS mean (SE)	12.14 (0.56)	12.41 (0.59)
95% CI of LS mean	(11.03, 13.25)	(11.24, 13.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.27 (-1.34, 1.89)
Absolute Change at Week 24 (MMRM)		
n	77	68
LS mean (SE)	0.51 (0.43)	0.40 (0.46)
95% CI of LS mean	(-0.34, 1.36)	(-0.50, 1.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-1.34, 1.14)
Week 52		
n	76	71
Mean (SD)	12.13 (4.44)	11.04 (4.12)
Absolute Change at Week 52		
n	74	68
Mean (SD)	0.28 (3.89)	-0.91 (4.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52 (MMRM)		
n	75	68
LS mean (SE)	11.92 (0.49)	11.30 (0.51)
95% CI of LS mean	(10.95, 12.88)	(10.28, 12.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.62 (-2.02, 0.79)
Absolute Change at Week 52 (MMRM)		
n	73	65
LS mean (SE)	0.22 (0.50)	-0.70 (0.53)
95% CI of LS mean	(-0.78, 1.21)	(-1.76, 0.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.92 (-2.37, 0.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	78	68
LS mean (SE)	0.36 (0.38)	-0.15 (0.40)
95% CI of LS mean	(-0.38, 1.11)	(-0.94, 0.64)
P-value within Treatment	0.3374	0.7105
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.51 (-1.60, 0.58)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3543
Hedges' G (SE)		-0.15 (0.17)
Hedges' 95% CI		(-0.48, 0.17)
Hedges' P-value		0.3545

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	11.31 (3.69)	11.25 (4.01)
Week 4 (MMRM)		
n	85	84
LS mean (SE)	11.50 (0.46)	11.19 (0.46)
95% CI of LS mean	(10.60, 12.40)	(10.28, 12.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-1.59, 0.98)
Absolute Change at Week 4 (MMRM)		
n	82	82
LS mean (SE)	0.08 (0.32)	-0.01 (0.32)
95% CI of LS mean	(-0.54, 0.70)	(-0.63, 0.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.97, 0.79)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 24 (MMRM)		
n	88	82
LS mean (SE)	11.88 (0.53)	11.83 (0.54)
95% CI of LS mean	(10.84, 12.92)	(10.76, 12.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-1.55, 1.44)
Absolute Change at Week 24 (MMRM)		
n	86	80
LS mean (SE)	0.52 (0.36)	0.73 (0.37)
95% CI of LS mean	(-0.20, 1.23)	(-0.01, 1.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.22 (-0.81, 1.25)
Week 52		
n	85	78
Mean (SD)	11.55 (4.28)	11.85 (4.29)
Absolute Change at Week 52		
n	82	76
Mean (SD)	0.02 (3.22)	0.43 (2.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52 (MMRM)		
n	84	77
LS mean (SE)	11.44 (0.45)	11.78 (0.47)
95% CI of LS mean	(10.54, 12.34)	(10.85, 12.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.34 (-0.95, 1.63)
Absolute Change at Week 52 (MMRM)		
n	81	75
LS mean (SE)	-0.03 (0.34)	0.47 (0.35)
95% CI of LS mean	(-0.71, 0.64)	(-0.23, 1.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-0.47, 1.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	86	80
LS mean (SE)	0.24 (0.27)	0.60 (0.28)
95% CI of LS mean	(-0.30, 0.78)	(0.05, 1.16)
P-value within Treatment	0.3761	0.0340
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-0.41, 1.13)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3591
Hedges' G (SE)		0.14 (0.15)
Hedges' 95% CI		(-0.16, 0.45)
Hedges' P-value		0.3593

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	108	105
Mean (SD)	11.57 (4.58)	11.56 (4.76)
Week 4 (MMRM)		
n	105	105
LS mean (SE)	11.48 (0.39)	11.21 (0.39)
95% CI of LS mean	(10.72, 12.24)	(10.45, 11.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.27 (-1.34, 0.81)
Absolute Change at Week 4 (MMRM)		
n	102	101
LS mean (SE)	0.18 (0.33)	-0.44 (0.33)
95% CI of LS mean	(-0.47, 0.82)	(-1.09, 0.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.61 (-1.53, 0.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 24 (MMRM)		
n	105	96
LS mean (SE)	11.71 (0.41)	11.10 (0.42)
95% CI of LS mean	(10.91, 12.51)	(10.27, 11.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.61 (-1.76, 0.54)
Absolute Change at Week 24 (MMRM)		
n	102	94
LS mean (SE)	0.37 (0.34)	-0.60 (0.35)
95% CI of LS mean	(-0.30, 1.03)	(-1.29, 0.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.97 (-1.92, -0.01)
Week 52		
n	103	103
Mean (SD)	11.62 (4.15)	10.76 (3.88)
Absolute Change at Week 52		
n	100	99
Mean (SD)	0.22 (3.30)	-0.85 (4.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52 (MMRM)		
n	102	101
LS mean (SE)	11.59 (0.39)	10.92 (0.39)
95% CI of LS mean	(10.82, 12.35)	(10.15, 11.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.66 (-1.75, 0.42)
Absolute Change at Week 52 (MMRM)		
n	99	97
LS mean (SE)	0.25 (0.38)	-0.70 (0.39)
95% CI of LS mean	(-0.51, 1.01)	(-1.47, 0.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.95 (-2.03, 0.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	103	99
LS mean (SE)	0.31 (0.31)	-0.65 (0.31)
95% CI of LS mean	(-0.30, 0.91)	(-1.27, -0.03)
P-value within Treatment	0.3174	0.0393
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.96 (-1.83, -0.09)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0302
Hedges' G (SE)		-0.31 (0.14)
Hedges' 95% CI		(-0.58, -0.03)
Hedges' P-value		0.0311

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	109	99
Mean (SD)	5.60 (2.72)	5.51 (2.41)
Week 4 (MMRM)		
n	109	98
LS mean (SE)	5.40 (0.22)	5.34 (0.23)
95% CI of LS mean	(4.98, 5.83)	(4.88, 5.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-0.69, 0.56)
Absolute Change at Week 4 (MMRM)		
n	104	96
LS mean (SE)	-0.17 (0.17)	-0.12 (0.18)
95% CI of LS mean	(-0.50, 0.17)	(-0.47, 0.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-0.44, 0.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 24 (MMRM)		
n	112	94
LS mean (SE)	5.63 (0.25)	5.72 (0.27)
95% CI of LS mean	(5.13, 6.12)	(5.19, 6.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-0.63, 0.83)
Absolute Change at Week 24 (MMRM)		
n	108	92
LS mean (SE)	0.08 (0.20)	0.26 (0.21)
95% CI of LS mean	(-0.31, 0.47)	(-0.16, 0.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-0.39, 0.76)
Week 52		
n	111	93
Mean (SD)	5.44 (2.72)	5.41 (2.66)
Absolute Change at Week 52		
n	106	91
Mean (SD)	-0.09 (1.55)	-0.13 (2.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52 (MMRM)		
n	111	92
LS mean (SE)	5.46 (0.25)	5.37 (0.27)
95% CI of LS mean	(4.96, 5.95)	(4.83, 5.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.82, 0.64)
Absolute Change at Week 52 (MMRM)		
n	106	90
LS mean (SE)	-0.10 (0.20)	-0.11 (0.21)
95% CI of LS mean	(-0.48, 0.29)	(-0.52, 0.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.01 (-0.58, 0.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	108	94
LS mean (SE)	-0.01 (0.18)	0.08 (0.19)
95% CI of LS mean	(-0.35, 0.34)	(-0.29, 0.45)
P-value within Treatment	0.9678	0.6760
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.09 (-0.42, 0.59)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7397
Hedges' G (SE)		0.05 (0.14)
Hedges' 95% CI		(-0.23, 0.32)
Hedges' P-value		0.7391

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	86	89
Mean (SD)	5.13 (2.00)	4.99 (1.97)
Week 4 (MMRM)		
n	82	91
LS mean (SE)	4.93 (0.20)	4.93 (0.19)
95% CI of LS mean	(4.53, 5.33)	(4.54, 5.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.01 (-0.56, 0.55)
Absolute Change at Week 4 (MMRM)		
n	81	88
LS mean (SE)	-0.21 (0.15)	-0.08 (0.14)
95% CI of LS mean	(-0.51, 0.08)	(-0.37, 0.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-0.28, 0.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 24 (MMRM)		
n	81	84
LS mean (SE)	4.93 (0.20)	4.79 (0.20)
95% CI of LS mean	(4.54, 5.33)	(4.40, 5.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-0.70, 0.41)
Absolute Change at Week 24 (MMRM)		
n	80	82
LS mean (SE)	-0.20 (0.20)	-0.19 (0.20)
95% CI of LS mean	(-0.60, 0.19)	(-0.58, 0.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-0.55, 0.56)
Week 52		
n	76	86
Mean (SD)	4.78 (1.51)	4.88 (1.75)
Absolute Change at Week 52		
n	75	83
Mean (SD)	-0.47 (1.47)	-0.13 (1.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52 (MMRM)		
n	75	86
LS mean (SE)	4.78 (0.18)	4.85 (0.17)
95% CI of LS mean	(4.43, 5.14)	(4.51, 5.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-0.42, 0.56)
Absolute Change at Week 52 (MMRM)		
n	74	83
LS mean (SE)	-0.38 (0.18)	-0.14 (0.17)
95% CI of LS mean	(-0.73, -0.03)	(-0.47, 0.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.24 (-0.24, 0.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	81	86
LS mean (SE)	-0.29 (0.17)	-0.17 (0.16)
95% CI of LS mean	(-0.62, 0.04)	(-0.49, 0.16)
P-value within Treatment	0.0870	0.3105
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-0.34, 0.59)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5990
Hedges' G (SE)		0.08 (0.15)
Hedges' 95% CI		(-0.22, 0.39)
Hedges' P-value		0.5991

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	30	25
Mean (SD)	5.40 (1.65)	5.24 (2.55)
Week 4 (MMRM)		
n	29	25
LS mean (SE)	5.04 (0.31)	4.76 (0.33)
95% CI of LS mean	(4.43, 5.66)	(4.09, 5.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.28 (-1.20, 0.63)
Absolute Change at Week 4 (MMRM)		
n	28	24
LS mean (SE)	-0.33 (0.28)	-0.65 (0.30)
95% CI of LS mean	(-0.89, 0.22)	(-1.25, -0.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-1.14, 0.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 24 (MMRM)		
n	28	23
LS mean (SE)	5.21 (0.35)	4.74 (0.39)
95% CI of LS mean	(4.51, 5.92)	(3.96, 5.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.48 (-1.53, 0.57)
Absolute Change at Week 24 (MMRM)		
n	27	22
LS mean (SE)	-0.17 (0.37)	-0.51 (0.41)
95% CI of LS mean	(-0.91, 0.57)	(-1.33, 0.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.35 (-1.45, 0.76)
Week 52		
n	27	24
Mean (SD)	4.96 (1.65)	4.58 (1.53)
Absolute Change at Week 52		
n	26	23
Mean (SD)	-0.42 (1.65)	-0.70 (1.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52 (MMRM)		
n	27	23
LS mean (SE)	4.97 (0.30)	4.59 (0.33)
95% CI of LS mean	(4.37, 5.58)	(3.93, 5.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-1.29, 0.52)
Absolute Change at Week 52 (MMRM)		
n	26	22
LS mean (SE)	-0.39 (0.35)	-0.69 (0.38)
95% CI of LS mean	(-1.09, 0.30)	(-1.46, 0.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-1.34, 0.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	27	23
LS mean (SE)	-0.28 (0.33)	-0.60 (0.36)
95% CI of LS mean	(-0.94, 0.38)	(-1.32, 0.12)
P-value within Treatment	0.3948	0.0983
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.32 (-1.30, 0.65)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5098
Hedges' G (SE)		-0.19 (0.28)
Hedges' 95% CI		(-0.75, 0.38)
Hedges' P-value		0.5092

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	166	166
Mean (SD)	5.38 (2.55)	5.24 (2.17)
Week 4 (MMRM)		
n	162	164
LS mean (SE)	5.21 (0.17)	5.21 (0.17)
95% CI of LS mean	(4.88, 5.53)	(4.88, 5.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-0.46, 0.47)
Absolute Change at Week 4 (MMRM)		
n	157	160
LS mean (SE)	-0.17 (0.13)	-0.01 (0.13)
95% CI of LS mean	(-0.42, 0.08)	(-0.25, 0.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-0.19, 0.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 24 (MMRM)		
n	165	155
LS mean (SE)	5.33 (0.18)	5.38 (0.19)
95% CI of LS mean	(4.97, 5.69)	(5.01, 5.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-0.47, 0.57)
Absolute Change at Week 24 (MMRM)		
n	161	152
LS mean (SE)	-0.03 (0.15)	0.14 (0.16)
95% CI of LS mean	(-0.33, 0.27)	(-0.17, 0.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-0.26, 0.60)
Week 52		
n	161	157
Mean (SD)	5.20 (2.42)	5.23 (2.36)
Absolute Change at Week 52		
n	156	153
Mean (SD)	-0.22 (1.50)	-0.05 (2.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52 (MMRM)		
n	159	155
LS mean (SE)	5.18 (0.18)	5.22 (0.18)
95% CI of LS mean	(4.82, 5.54)	(4.86, 5.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.04 (-0.47, 0.54)
Absolute Change at Week 52 (MMRM)		
n	154	151
LS mean (SE)	-0.19 (0.15)	-0.03 (0.15)
95% CI of LS mean	(-0.48, 0.10)	(-0.32, 0.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-0.24, 0.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	162	157
LS mean (SE)	-0.11 (0.13)	0.06 (0.13)
95% CI of LS mean	(-0.37, 0.15)	(-0.21, 0.32)
P-value within Treatment	0.4019	0.6782
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-0.21, 0.54)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3769
Hedges' G (SE)		0.10 (0.11)
Hedges' 95% CI		(-0.12, 0.32)
Hedges' P-value		0.3770

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	17	17
Mean (SD)	5.41 (2.03)	5.88 (2.89)
Week 4 (MMRM)		
n	18	16
LS mean (SE)	5.44 (0.45)	5.28 (0.49)
95% CI of LS mean	(4.51, 6.36)	(4.28, 6.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-1.54, 1.23)
Absolute Change at Week 4 (MMRM)		
n	16	16
LS mean (SE)	-0.27 (0.50)	-0.86 (0.50)
95% CI of LS mean	(-1.29, 0.74)	(-1.89, 0.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.59 (-2.07, 0.89)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 24 (MMRM)		
n	18	15
LS mean (SE)	5.56 (0.58)	5.94 (0.64)
95% CI of LS mean	(4.34, 6.78)	(4.60, 7.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.38 (-1.46, 2.21)
Absolute Change at Week 24 (MMRM)		
n	17	15
LS mean (SE)	-0.01 (0.56)	-0.11 (0.59)
95% CI of LS mean	(-1.16, 1.13)	(-1.32, 1.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-1.79, 1.60)
Week 52		
n	17	13
Mean (SD)	5.18 (1.88)	6.08 (3.28)
Absolute Change at Week 52		
n	15	13
Mean (SD)	-0.60 (1.68)	-0.23 (3.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52 (MMRM)		
n	17	13
LS mean (SE)	5.06 (0.62)	6.11 (0.70)
95% CI of LS mean	(3.80, 6.33)	(4.67, 7.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.05 (-0.89, 2.98)
Absolute Change at Week 52 (MMRM)		
n	15	13
LS mean (SE)	-0.53 (0.68)	-0.11 (0.72)
95% CI of LS mean	(-1.92, 0.86)	(-1.59, 1.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.42 (-1.64, 2.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	17	16
LS mean (SE)	-0.27 (0.52)	-0.11 (0.55)
95% CI of LS mean	(-1.34, 0.80)	(-1.24, 1.02)
P-value within Treatment	0.6106	0.8467
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-1.43, 1.75)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8357
Hedges' G (SE)		0.07 (0.34)
Hedges' 95% CI		(-0.62, 0.77)
Hedges' P-value		0.8323

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	178	172
Mean (SD)	5.39 (2.47)	5.17 (2.14)
Week 4 (MMRM)		
n	173	173
LS mean (SE)	5.15 (0.16)	5.15 (0.16)
95% CI of LS mean	(4.85, 5.46)	(4.84, 5.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.01 (-0.44, 0.43)
Absolute Change at Week 4 (MMRM)		
n	169	168
LS mean (SE)	-0.17 (0.12)	-0.03 (0.12)
95% CI of LS mean	(-0.40, 0.06)	(-0.27, 0.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-0.19, 0.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 24 (MMRM)		
n	175	163
LS mean (SE)	5.28 (0.17)	5.23 (0.18)
95% CI of LS mean	(4.94, 5.62)	(4.88, 5.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-0.54, 0.44)
Absolute Change at Week 24 (MMRM)		
n	171	159
LS mean (SE)	-0.04 (0.15)	0.04 (0.15)
95% CI of LS mean	(-0.33, 0.25)	(-0.25, 0.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.09 (-0.33, 0.50)
Week 52		
n	170	167
Mean (SD)	5.17 (2.37)	5.05 (2.16)
Absolute Change at Week 52		
n	166	162
Mean (SD)	-0.22 (1.51)	-0.14 (1.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52 (MMRM)		
n	169	165
LS mean (SE)	5.15 (0.17)	5.06 (0.17)
95% CI of LS mean	(4.82, 5.48)	(4.73, 5.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.56, 0.39)
Absolute Change at Week 52 (MMRM)		
n	165	160
LS mean (SE)	-0.18 (0.13)	-0.12 (0.14)
95% CI of LS mean	(-0.44, 0.08)	(-0.39, 0.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.06 (-0.32, 0.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	172	164
LS mean (SE)	-0.11 (0.13)	-0.04 (0.13)
95% CI of LS mean	(-0.36, 0.14)	(-0.29, 0.22)
P-value within Treatment	0.3810	0.7677
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-0.28, 0.43)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6879
Hedges' G (SE)		0.04 (0.11)
Hedges' 95% CI		(-0.17, 0.26)
Hedges' P-value		0.6878

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	115	114
Mean (SD)	5.38 (2.41)	5.02 (1.80)
Week 4 (MMRM)		
n	112	114
LS mean (SE)	5.14 (0.19)	5.05 (0.19)
95% CI of LS mean	(4.75, 5.52)	(4.67, 5.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.63, 0.45)
Absolute Change at Week 4 (MMRM)		
n	108	112
LS mean (SE)	-0.17 (0.13)	0.07 (0.13)
95% CI of LS mean	(-0.43, 0.09)	(-0.18, 0.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.25 (-0.12, 0.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 24 (MMRM)		
n	115	108
LS mean (SE)	5.37 (0.21)	5.16 (0.22)
95% CI of LS mean	(4.95, 5.79)	(4.73, 5.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.21 (-0.81, 0.39)
Absolute Change at Week 24 (MMRM)		
n	111	106
LS mean (SE)	0.06 (0.16)	0.18 (0.16)
95% CI of LS mean	(-0.26, 0.38)	(-0.15, 0.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.11 (-0.34, 0.57)
Week 52		
n	112	110
Mean (SD)	5.19 (2.32)	5.17 (2.22)
Absolute Change at Week 52		
n	108	108
Mean (SD)	-0.15 (1.24)	0.14 (1.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52 (MMRM)		
n	111	110
LS mean (SE)	5.20 (0.20)	5.11 (0.21)
95% CI of LS mean	(4.80, 5.61)	(4.71, 5.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.67, 0.48)
Absolute Change at Week 52 (MMRM)		
n	107	108
LS mean (SE)	-0.12 (0.14)	0.12 (0.13)
95% CI of LS mean	(-0.39, 0.14)	(-0.14, 0.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.25 (-0.13, 0.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	112
LS mean (SE)	-0.03 (0.13)	0.15 (0.13)
95% CI of LS mean	(-0.29, 0.23)	(-0.11, 0.41)
P-value within Treatment	0.8208	0.2594
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-0.19, 0.55)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3395
Hedges' G (SE)		0.13 (0.13)
Hedges' 95% CI		(-0.14, 0.39)
Hedges' P-value		0.3386

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	81	77
Mean (SD)	5.38 (2.47)	5.57 (2.69)
Week 4 (MMRM)		
n	79	75
LS mean (SE)	5.26 (0.24)	5.30 (0.24)
95% CI of LS mean	(4.79, 5.72)	(4.81, 5.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.04 (-0.63, 0.71)
Absolute Change at Week 4 (MMRM)		
n	77	72
LS mean (SE)	-0.24 (0.21)	-0.34 (0.21)
95% CI of LS mean	(-0.65, 0.16)	(-0.76, 0.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-0.68, 0.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 24 (MMRM)		
n	78	70
LS mean (SE)	5.24 (0.27)	5.50 (0.28)
95% CI of LS mean	(4.71, 5.76)	(4.95, 6.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.26 (-0.50, 1.03)
Absolute Change at Week 24 (MMRM)		
n	77	68
LS mean (SE)	-0.23 (0.26)	-0.10 (0.27)
95% CI of LS mean	(-0.74, 0.28)	(-0.64, 0.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-0.61, 0.88)
Week 52		
n	76	71
Mean (SD)	5.13 (2.34)	5.10 (2.36)
Absolute Change at Week 52		
n	74	68
Mean (SD)	-0.39 (1.85)	-0.56 (2.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52 (MMRM)		
n	75	68
LS mean (SE)	5.09 (0.26)	5.15 (0.28)
95% CI of LS mean	(4.57, 5.62)	(4.60, 5.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-0.70, 0.81)
Absolute Change at Week 52 (MMRM)		
n	73	65
LS mean (SE)	-0.38 (0.27)	-0.45 (0.28)
95% CI of LS mean	(-0.91, 0.15)	(-1.01, 0.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-0.84, 0.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	78	68
LS mean (SE)	-0.31 (0.23)	-0.28 (0.25)
95% CI of LS mean	(-0.77, 0.16)	(-0.77, 0.21)
P-value within Treatment	0.1915	0.2681
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.03 (-0.64, 0.71)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9271
Hedges' G (SE)		0.02 (0.17)
Hedges' 95% CI		(-0.31, 0.34)
Hedges' P-value		0.9270

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	5.22 (2.01)	5.09 (1.89)
Week 4 (MMRM)		
n	85	84
LS mean (SE)	5.10 (0.21)	5.04 (0.21)
95% CI of LS mean	(4.68, 5.51)	(4.62, 5.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-0.65, 0.54)
Absolute Change at Week 4 (MMRM)		
n	82	82
LS mean (SE)	-0.20 (0.16)	-0.04 (0.16)
95% CI of LS mean	(-0.51, 0.12)	(-0.35, 0.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-0.29, 0.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 24 (MMRM)		
n	88	82
LS mean (SE)	5.23 (0.24)	5.44 (0.25)
95% CI of LS mean	(4.75, 5.71)	(4.94, 5.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.21 (-0.48, 0.90)
Absolute Change at Week 24 (MMRM)		
n	86	80
LS mean (SE)	-0.03 (0.21)	0.36 (0.21)
95% CI of LS mean	(-0.44, 0.38)	(-0.07, 0.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.39 (-0.20, 0.98)
Week 52		
n	85	78
Mean (SD)	5.14 (1.90)	5.14 (1.95)
Absolute Change at Week 52		
n	82	76
Mean (SD)	-0.18 (1.54)	0.03 (1.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52 (MMRM)		
n	84	77
LS mean (SE)	5.13 (0.20)	5.09 (0.21)
95% CI of LS mean	(4.74, 5.53)	(4.68, 5.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-0.61, 0.52)
Absolute Change at Week 52 (MMRM)		
n	81	75
LS mean (SE)	-0.15 (0.17)	0.00 (0.18)
95% CI of LS mean	(-0.49, 0.19)	(-0.35, 0.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-0.34, 0.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	86	80
LS mean (SE)	-0.09 (0.17)	0.18 (0.17)
95% CI of LS mean	(-0.42, 0.23)	(-0.16, 0.52)
P-value within Treatment	0.5793	0.2927
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.27 (-0.20, 0.74)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2546
Hedges' G (SE)		0.18 (0.15)
Hedges' 95% CI		(-0.13, 0.48)
Hedges' P-value		0.2551

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	108	106
Mean (SD)	5.52 (2.73)	5.36 (2.44)
Week 4 (MMRM)		
n	106	105
LS mean (SE)	5.25 (0.21)	5.24 (0.21)
95% CI of LS mean	(4.83, 5.66)	(4.82, 5.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.01 (-0.60, 0.58)
Absolute Change at Week 4 (MMRM)		
n	103	102
LS mean (SE)	-0.18 (0.16)	-0.15 (0.17)
95% CI of LS mean	(-0.50, 0.15)	(-0.48, 0.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.03 (-0.43, 0.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 24 (MMRM)		
n	105	96
LS mean (SE)	5.38 (0.23)	5.17 (0.23)
95% CI of LS mean	(4.93, 5.83)	(4.71, 5.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.21 (-0.85, 0.43)
Absolute Change at Week 24 (MMRM)		
n	102	94
LS mean (SE)	-0.05 (0.19)	-0.21 (0.20)
95% CI of LS mean	(-0.44, 0.33)	(-0.60, 0.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.16 (-0.70, 0.39)
Week 52		
n	103	103
Mean (SD)	5.18 (2.63)	5.15 (2.49)
Absolute Change at Week 52		
n	100	100
Mean (SD)	-0.30 (1.51)	-0.25 (2.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52 (MMRM)		
n	102	101
LS mean (SE)	5.17 (0.24)	5.17 (0.25)
95% CI of LS mean	(4.69, 5.65)	(4.69, 5.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-0.68, 0.69)
Absolute Change at Week 52 (MMRM)		
n	99	98
LS mean (SE)	-0.27 (0.20)	-0.22 (0.20)
95% CI of LS mean	(-0.66, 0.13)	(-0.62, 0.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-0.51, 0.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	103	100
LS mean (SE)	-0.16 (0.18)	-0.22 (0.18)
95% CI of LS mean	(-0.51, 0.19)	(-0.57, 0.14)
P-value within Treatment	0.3678	0.2324
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-0.56, 0.44)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8251
Hedges' G (SE)		-0.03 (0.14)
Hedges' 95% CI		(-0.31, 0.24)
Hedges' P-value		0.8250

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	109	99
Mean (SD)	7.44 (3.47)	7.21 (3.08)
Week 4 (MMRM)		
n	110	98
LS mean (SE)	7.30 (0.28)	7.04 (0.29)
95% CI of LS mean	(6.76, 7.85)	(6.46, 7.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.27 (-1.06, 0.53)
Absolute Change at Week 4 (MMRM)		
n	105	96
LS mean (SE)	-0.10 (0.21)	-0.10 (0.22)
95% CI of LS mean	(-0.52, 0.31)	(-0.53, 0.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-0.59, 0.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 24 (MMRM)		
n	112	94
LS mean (SE)	7.35 (0.30)	7.25 (0.32)
95% CI of LS mean	(6.76, 7.93)	(6.62, 7.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.95, 0.77)
Absolute Change at Week 24 (MMRM)		
n	108	92
LS mean (SE)	-0.04 (0.29)	0.14 (0.31)
95% CI of LS mean	(-0.61, 0.53)	(-0.47, 0.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-0.65, 1.02)
Week 52		
n	111	93
Mean (SD)	7.14 (3.38)	7.08 (3.00)
Absolute Change at Week 52		
n	106	91
Mean (SD)	-0.26 (2.18)	-0.14 (2.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52 (MMRM)		
n	111	92
LS mean (SE)	7.15 (0.30)	7.09 (0.33)
95% CI of LS mean	(6.55, 7.75)	(6.44, 7.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-0.94, 0.83)
Absolute Change at Week 52 (MMRM)		
n	106	90
LS mean (SE)	-0.28 (0.25)	-0.05 (0.27)
95% CI of LS mean	(-0.78, 0.23)	(-0.59, 0.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.23 (-0.51, 0.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	108	94
LS mean (SE)	-0.16 (0.24)	0.04 (0.26)
95% CI of LS mean	(-0.63, 0.31)	(-0.46, 0.55)
P-value within Treatment	0.5082	0.8623
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.20 (-0.49, 0.90)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5641
Hedges' G (SE)		0.08 (0.14)
Hedges' 95% CI		(-0.20, 0.36)
Hedges' P-value		0.5634

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	86	89
Mean (SD)	7.00 (2.69)	6.73 (2.78)
Week 4 (MMRM)		
n	82	92
LS mean (SE)	6.68 (0.28)	6.76 (0.27)
95% CI of LS mean	(6.12, 7.24)	(6.22, 7.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-0.69, 0.86)
Absolute Change at Week 4 (MMRM)		
n	81	89
LS mean (SE)	-0.24 (0.20)	-0.11 (0.19)
95% CI of LS mean	(-0.64, 0.16)	(-0.49, 0.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-0.42, 0.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 24 (MMRM)		
n	81	85
LS mean (SE)	6.97 (0.32)	6.57 (0.31)
95% CI of LS mean	(6.35, 7.59)	(5.96, 7.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.40 (-1.27, 0.46)
Absolute Change at Week 24 (MMRM)		
n	80	83
LS mean (SE)	0.06 (0.27)	-0.12 (0.26)
95% CI of LS mean	(-0.47, 0.59)	(-0.64, 0.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-0.92, 0.56)
Week 52		
n	76	86
Mean (SD)	6.62 (2.18)	6.45 (2.28)
Absolute Change at Week 52		
n	75	83
Mean (SD)	-0.47 (2.30)	-0.35 (2.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52 (MMRM)		
n	75	86
LS mean (SE)	6.60 (0.25)	6.44 (0.24)
95% CI of LS mean	(6.10, 7.09)	(5.97, 6.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-0.84, 0.53)
Absolute Change at Week 52 (MMRM)		
n	74	83
LS mean (SE)	-0.39 (0.28)	-0.33 (0.27)
95% CI of LS mean	(-0.94, 0.16)	(-0.86, 0.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.06 (-0.70, 0.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	81	86
LS mean (SE)	-0.17 (0.24)	-0.23 (0.23)
95% CI of LS mean	(-0.64, 0.31)	(-0.68, 0.23)
P-value within Treatment	0.4884	0.3310
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-0.72, 0.60)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8586
Hedges' G (SE)		-0.03 (0.15)
Hedges' 95% CI		(-0.33, 0.28)
Hedges' P-value		0.8585

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	30	25
Mean (SD)	7.40 (2.84)	6.80 (2.87)
Week 4 (MMRM)		
n	29	25
LS mean (SE)	6.89 (0.53)	7.07 (0.58)
95% CI of LS mean	(5.82, 7.96)	(5.91, 8.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-1.40, 1.76)
Absolute Change at Week 4 (MMRM)		
n	28	24
LS mean (SE)	-0.21 (0.41)	-0.17 (0.45)
95% CI of LS mean	(-1.04, 0.62)	(-1.07, 0.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.04 (-1.18, 1.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 24 (MMRM)		
n	28	23
LS mean (SE)	7.19 (0.51)	6.54 (0.56)
95% CI of LS mean	(6.16, 8.22)	(5.41, 7.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.66 (-2.19, 0.88)
Absolute Change at Week 24 (MMRM)		
n	27	22
LS mean (SE)	0.10 (0.51)	-0.27 (0.56)
95% CI of LS mean	(-0.93, 1.13)	(-1.40, 0.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.37 (-1.90, 1.16)
Week 52		
n	27	24
Mean (SD)	7.11 (2.29)	6.63 (3.03)
Absolute Change at Week 52		
n	26	23
Mean (SD)	-0.04 (2.42)	-0.35 (2.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52 (MMRM)		
n	27	23
LS mean (SE)	7.12 (0.50)	6.73 (0.55)
95% CI of LS mean	(6.12, 8.13)	(5.64, 7.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.39 (-1.89, 1.11)
Absolute Change at Week 52 (MMRM)		
n	26	22
LS mean (SE)	-0.04 (0.52)	-0.26 (0.56)
95% CI of LS mean	(-1.07, 1.00)	(-1.39, 0.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-1.76, 1.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	27	23
LS mean (SE)	0.03 (0.47)	-0.26 (0.52)
95% CI of LS mean	(-0.92, 0.99)	(-1.30, 0.78)
P-value within Treatment	0.9437	0.6154
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-1.71, 1.12)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6767
Hedges' G (SE)		-0.12 (0.28)
Hedges' 95% CI		(-0.68, 0.44)
Hedges' P-value		0.6759

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	166	166
Mean (SD)	7.20 (3.20)	6.98 (2.95)
Week 4 (MMRM)		
n	163	165
LS mean (SE)	7.04 (0.21)	6.89 (0.21)
95% CI of LS mean	(6.62, 7.46)	(6.47, 7.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-0.75, 0.45)
Absolute Change at Week 4 (MMRM)		
n	158	161
LS mean (SE)	-0.16 (0.16)	-0.10 (0.16)
95% CI of LS mean	(-0.46, 0.15)	(-0.41, 0.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.06 (-0.38, 0.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 24 (MMRM)		
n	165	156
LS mean (SE)	7.18 (0.24)	6.98 (0.24)
95% CI of LS mean	(6.71, 7.65)	(6.50, 7.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.19 (-0.86, 0.48)
Absolute Change at Week 24 (MMRM)		
n	161	153
LS mean (SE)	-0.01 (0.22)	0.04 (0.22)
95% CI of LS mean	(-0.44, 0.41)	(-0.40, 0.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-0.56, 0.66)
Week 52		
n	161	157
Mean (SD)	6.89 (3.05)	6.78 (2.64)
Absolute Change at Week 52		
n	156	153
Mean (SD)	-0.38 (2.20)	-0.22 (2.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52 (MMRM)		
n	159	155
LS mean (SE)	6.86 (0.22)	6.79 (0.22)
95% CI of LS mean	(6.42, 7.29)	(6.35, 7.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-0.68, 0.55)
Absolute Change at Week 52 (MMRM)		
n	154	151
LS mean (SE)	-0.37 (0.20)	-0.18 (0.20)
95% CI of LS mean	(-0.77, 0.02)	(-0.58, 0.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.20 (-0.36, 0.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	162	157
LS mean (SE)	-0.19 (0.18)	-0.07 (0.18)
95% CI of LS mean	(-0.55, 0.16)	(-0.43, 0.29)
P-value within Treatment	0.2857	0.7064
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-0.38, 0.63)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6296
Hedges' G (SE)		0.05 (0.11)
Hedges' 95% CI		(-0.17, 0.27)
Hedges' P-value		0.6295

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	17	17
Mean (SD)	6.94 (2.14)	7.41 (3.37)
Week 4 (MMRM)		
n	19	16
LS mean (SE)	7.18 (0.68)	7.16 (0.75)
95% CI of LS mean	(5.79, 8.58)	(5.63, 8.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-2.12, 2.07)
Absolute Change at Week 4 (MMRM)		
n	17	16
LS mean (SE)	0.03 (0.54)	-0.53 (0.55)
95% CI of LS mean	(-1.07, 1.13)	(-1.67, 0.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.56 (-2.16, 1.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 24 (MMRM)		
n	18	15
LS mean (SE)	7.24 (0.88)	8.31 (0.96)
95% CI of LS mean	(5.40, 9.08)	(6.30, 10.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.08 (-1.67, 3.83)
Absolute Change at Week 24 (MMRM)		
n	17	15
LS mean (SE)	-0.03 (0.59)	0.59 (0.63)
95% CI of LS mean	(-1.24, 1.19)	(-0.71, 1.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.62 (-1.17, 2.40)
Week 52		
n	17	13
Mean (SD)	7.18 (3.11)	7.69 (2.98)
Absolute Change at Week 52		
n	15	13
Mean (SD)	-0.20 (2.54)	-0.23 (2.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52 (MMRM)		
n	17	13
LS mean (SE)	6.82 (0.73)	7.77 (0.83)
95% CI of LS mean	(5.32, 8.31)	(6.08, 9.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.96 (-1.32, 3.23)
Absolute Change at Week 52 (MMRM)		
n	15	13
LS mean (SE)	-0.37 (0.70)	-0.26 (0.75)
95% CI of LS mean	(-1.80, 1.07)	(-1.80, 1.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-2.01, 2.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	17	16
LS mean (SE)	-0.20 (0.45)	0.16 (0.48)
95% CI of LS mean	(-1.12, 0.72)	(-0.82, 1.14)
P-value within Treatment	0.6635	0.7354
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-1.00, 1.72)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5921
Hedges' G (SE)		0.19 (0.34)
Hedges' 95% CI		(-0.51, 0.88)
Hedges' P-value		0.5865

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	178	172
Mean (SD)	7.28 (3.23)	6.90 (2.90)
Week 4 (MMRM)		
n	173	174
LS mean (SE)	6.97 (0.21)	6.92 (0.21)
95% CI of LS mean	(6.57, 7.38)	(6.51, 7.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-0.63, 0.52)
Absolute Change at Week 4 (MMRM)		
n	169	169
LS mean (SE)	-0.20 (0.15)	-0.06 (0.15)
95% CI of LS mean	(-0.49, 0.10)	(-0.35, 0.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-0.28, 0.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 24 (MMRM)		
n	175	164
LS mean (SE)	7.16 (0.23)	6.82 (0.23)
95% CI of LS mean	(6.72, 7.61)	(6.36, 7.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.34 (-0.98, 0.29)
Absolute Change at Week 24 (MMRM)		
n	171	160
LS mean (SE)	-0.01 (0.21)	-0.06 (0.22)
95% CI of LS mean	(-0.43, 0.41)	(-0.49, 0.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-0.65, 0.55)
Week 52		
n	170	167
Mean (SD)	6.91 (2.95)	6.66 (2.65)
Absolute Change at Week 52		
n	166	162
Mean (SD)	-0.36 (2.21)	-0.24 (2.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52 (MMRM)		
n	169	165
LS mean (SE)	6.87 (0.21)	6.73 (0.21)
95% CI of LS mean	(6.45, 7.28)	(6.31, 7.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-0.73, 0.45)
Absolute Change at Week 52 (MMRM)		
n	165	160
LS mean (SE)	-0.33 (0.19)	-0.19 (0.20)
95% CI of LS mean	(-0.71, 0.05)	(-0.58, 0.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-0.40, 0.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	172	164
LS mean (SE)	-0.17 (0.18)	-0.12 (0.19)
95% CI of LS mean	(-0.52, 0.19)	(-0.49, 0.24)
P-value within Treatment	0.3562	0.5078
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.04 (-0.47, 0.55)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8631
Hedges' G (SE)		0.02 (0.11)
Hedges' 95% CI		(-0.20, 0.23)
Hedges' P-value		0.8631

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	115	114
Mean (SD)	7.00 (3.07)	6.75 (2.69)
Week 4 (MMRM)		
n	112	115
LS mean (SE)	6.67 (0.24)	6.66 (0.24)
95% CI of LS mean	(6.19, 7.14)	(6.18, 7.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.01 (-0.68, 0.67)
Absolute Change at Week 4 (MMRM)		
n	108	113
LS mean (SE)	-0.19 (0.17)	-0.07 (0.16)
95% CI of LS mean	(-0.52, 0.14)	(-0.39, 0.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-0.34, 0.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 24 (MMRM)		
n	115	109
LS mean (SE)	7.00 (0.27)	6.56 (0.27)
95% CI of LS mean	(6.47, 7.52)	(6.02, 7.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.44 (-1.19, 0.31)
Absolute Change at Week 24 (MMRM)		
n	111	107
LS mean (SE)	0.15 (0.24)	-0.11 (0.24)
95% CI of LS mean	(-0.32, 0.63)	(-0.59, 0.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-0.94, 0.41)
Week 52		
n	112	110
Mean (SD)	6.63 (2.73)	6.83 (2.86)
Absolute Change at Week 52		
n	108	108
Mean (SD)	-0.28 (2.05)	0.06 (2.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52 (MMRM)		
n	111	110
LS mean (SE)	6.64 (0.26)	6.77 (0.26)
95% CI of LS mean	(6.13, 7.15)	(6.26, 7.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-0.59, 0.86)
Absolute Change at Week 52 (MMRM)		
n	107	108
LS mean (SE)	-0.26 (0.22)	0.07 (0.22)
95% CI of LS mean	(-0.69, 0.17)	(-0.36, 0.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.33 (-0.28, 0.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	112
LS mean (SE)	-0.05 (0.20)	-0.02 (0.20)
95% CI of LS mean	(-0.45, 0.34)	(-0.42, 0.37)
P-value within Treatment	0.7896	0.9118
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.03 (-0.53, 0.59)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9123
Hedges' G (SE)		0.01 (0.13)
Hedges' 95% CI		(-0.25, 0.28)
Hedges' P-value		0.9121

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	81	77
Mean (SD)	7.57 (3.24)	7.26 (3.25)
Week 4 (MMRM)		
n	80	75
LS mean (SE)	7.52 (0.33)	7.31 (0.34)
95% CI of LS mean	(6.86, 8.17)	(6.63, 7.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.20 (-1.15, 0.74)
Absolute Change at Week 4 (MMRM)		
n	78	72
LS mean (SE)	-0.15 (0.27)	-0.15 (0.28)
95% CI of LS mean	(-0.67, 0.38)	(-0.69, 0.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-0.76, 0.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 24 (MMRM)		
n	78	70
LS mean (SE)	7.43 (0.37)	7.49 (0.38)
95% CI of LS mean	(6.71, 8.15)	(6.73, 8.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.06 (-0.99, 1.11)
Absolute Change at Week 24 (MMRM)		
n	77	68
LS mean (SE)	-0.24 (0.35)	0.21 (0.37)
95% CI of LS mean	(-0.92, 0.45)	(-0.52, 0.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.44 (-0.56, 1.44)
Week 52		
n	76	71
Mean (SD)	7.37 (3.21)	6.65 (2.40)
Absolute Change at Week 52		
n	74	68
Mean (SD)	-0.42 (2.47)	-0.72 (3.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52 (MMRM)		
n	75	68
LS mean (SE)	7.28 (0.32)	6.77 (0.34)
95% CI of LS mean	(6.64, 7.91)	(6.10, 7.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.51 (-1.43, 0.42)
Absolute Change at Week 52 (MMRM)		
n	73	65
LS mean (SE)	-0.43 (0.33)	-0.59 (0.35)
95% CI of LS mean	(-1.09, 0.22)	(-1.28, 0.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-1.11, 0.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	78	68
LS mean (SE)	-0.34 (0.30)	-0.19 (0.32)
95% CI of LS mean	(-0.93, 0.26)	(-0.82, 0.44)
P-value within Treatment	0.2652	0.5514
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-0.72, 1.01)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7404
Hedges' G (SE)		0.05 (0.17)
Hedges' 95% CI		(-0.27, 0.38)
Hedges' P-value		0.7403

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	6.94 (2.76)	6.98 (2.83)
Week 4 (MMRM)		
n	85	84
LS mean (SE)	6.90 (0.30)	7.04 (0.30)
95% CI of LS mean	(6.31, 7.49)	(6.45, 7.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-0.70, 0.99)
Absolute Change at Week 4 (MMRM)		
n	82	82
LS mean (SE)	-0.05 (0.17)	0.08 (0.17)
95% CI of LS mean	(-0.39, 0.28)	(-0.25, 0.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-0.34, 0.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 24 (MMRM)		
n	88	82
LS mean (SE)	7.14 (0.33)	7.14 (0.34)
95% CI of LS mean	(6.49, 7.79)	(6.47, 7.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-0.94, 0.93)
Absolute Change at Week 24 (MMRM)		
n	86	80
LS mean (SE)	0.20 (0.25)	0.25 (0.26)
95% CI of LS mean	(-0.30, 0.70)	(-0.26, 0.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-0.66, 0.77)
Week 52		
n	85	78
Mean (SD)	6.88 (2.43)	7.14 (3.11)
Absolute Change at Week 52		
n	82	76
Mean (SD)	-0.17 (1.71)	0.17 (2.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52 (MMRM)		
n	84	77
LS mean (SE)	6.80 (0.29)	7.12 (0.30)
95% CI of LS mean	(6.23, 7.38)	(6.52, 7.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.31 (-0.52, 1.15)
Absolute Change at Week 52 (MMRM)		
n	81	75
LS mean (SE)	-0.20 (0.24)	0.18 (0.25)
95% CI of LS mean	(-0.66, 0.27)	(-0.30, 0.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.38 (-0.29, 1.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	86	80
LS mean (SE)	0.00 (0.20)	0.22 (0.21)
95% CI of LS mean	(-0.40, 0.40)	(-0.20, 0.63)
P-value within Treatment	0.9935	0.2987
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.22 (-0.36, 0.79)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4585
Hedges' G (SE)		0.11 (0.15)
Hedges' 95% CI		(-0.19, 0.42)
Hedges' P-value		0.4585

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	108	106
Mean (SD)	7.47 (3.42)	6.93 (3.02)
Week 4 (MMRM)		
n	107	106
LS mean (SE)	7.10 (0.27)	6.83 (0.27)
95% CI of LS mean	(6.57, 7.63)	(6.29, 7.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.27 (-1.03, 0.48)
Absolute Change at Week 4 (MMRM)		
n	104	103
LS mean (SE)	-0.26 (0.22)	-0.26 (0.23)
95% CI of LS mean	(-0.70, 0.18)	(-0.70, 0.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-0.63, 0.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 24 (MMRM)		
n	105	97
LS mean (SE)	7.19 (0.29)	6.77 (0.30)
95% CI of LS mean	(6.62, 7.76)	(6.18, 7.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.42 (-1.23, 0.40)
Absolute Change at Week 24 (MMRM)		
n	102	95
LS mean (SE)	-0.16 (0.30)	-0.18 (0.31)
95% CI of LS mean	(-0.75, 0.43)	(-0.79, 0.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.02 (-0.87, 0.83)
Week 52		
n	103	103
Mean (SD)	6.96 (3.33)	6.47 (2.29)
Absolute Change at Week 52		
n	100	100
Mean (SD)	-0.47 (2.58)	-0.55 (2.89)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52 (MMRM)		
n	102	101
LS mean (SE)	6.96 (0.28)	6.53 (0.28)
95% CI of LS mean	(6.41, 7.50)	(5.98, 7.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.42 (-1.20, 0.35)
Absolute Change at Week 52 (MMRM)		
n	99	98
LS mean (SE)	-0.42 (0.28)	-0.49 (0.28)
95% CI of LS mean	(-0.97, 0.12)	(-1.04, 0.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-0.84, 0.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	103	100
LS mean (SE)	-0.29 (0.26)	-0.34 (0.26)
95% CI of LS mean	(-0.80, 0.22)	(-0.86, 0.18)
P-value within Treatment	0.2614	0.2048
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-0.77, 0.69)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9067
Hedges' G (SE)		-0.02 (0.14)
Hedges' 95% CI		(-0.29, 0.26)
Hedges' P-value		0.9066

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	109	99
Mean (SD)	5.43 (2.46)	5.36 (2.35)
Week 4 (MMRM)		
n	109	98
LS mean (SE)	5.01 (0.20)	5.07 (0.22)
95% CI of LS mean	(4.60, 5.41)	(4.64, 5.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-0.52, 0.66)
Absolute Change at Week 4 (MMRM)		
n	104	96
LS mean (SE)	-0.37 (0.16)	-0.22 (0.16)
95% CI of LS mean	(-0.68, -0.07)	(-0.54, 0.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-0.29, 0.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 24 (MMRM)		
n	112	94
LS mean (SE)	5.27 (0.23)	5.19 (0.24)
95% CI of LS mean	(4.83, 5.72)	(4.71, 5.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-0.74, 0.57)
Absolute Change at Week 24 (MMRM)		
n	108	92
LS mean (SE)	-0.12 (0.17)	-0.12 (0.18)
95% CI of LS mean	(-0.46, 0.22)	(-0.48, 0.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-0.49, 0.50)
Week 52		
n	111	93
Mean (SD)	5.12 (2.16)	5.04 (2.13)
Absolute Change at Week 52		
n	106	91
Mean (SD)	-0.21 (1.69)	-0.40 (2.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52 (MMRM)		
n	111	92
LS mean (SE)	5.16 (0.20)	5.00 (0.22)
95% CI of LS mean	(4.77, 5.55)	(4.57, 5.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.16 (-0.74, 0.42)
Absolute Change at Week 52 (MMRM)		
n	106	90
LS mean (SE)	-0.23 (0.18)	-0.33 (0.20)
95% CI of LS mean	(-0.60, 0.13)	(-0.73, 0.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-0.64, 0.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	108	94
LS mean (SE)	-0.18 (0.16)	-0.23 (0.17)
95% CI of LS mean	(-0.49, 0.13)	(-0.56, 0.11)
P-value within Treatment	0.2643	0.1846
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-0.51, 0.41)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8342
Hedges' G (SE)		-0.03 (0.14)
Hedges' 95% CI		(-0.31, 0.25)
Hedges' P-value		0.8337

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	86	88
Mean (SD)	4.59 (1.85)	4.57 (1.73)
Week 4 (MMRM)		
n	82	91
LS mean (SE)	4.87 (0.20)	4.49 (0.19)
95% CI of LS mean	(4.49, 5.26)	(4.12, 4.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.39 (-0.92, 0.15)
Absolute Change at Week 4 (MMRM)		
n	81	87
LS mean (SE)	0.29 (0.13)	-0.14 (0.13)
95% CI of LS mean	(0.03, 0.54)	(-0.39, 0.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.43 (-0.78, -0.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 24 (MMRM)		
n	81	84
LS mean (SE)	4.81 (0.21)	4.59 (0.21)
95% CI of LS mean	(4.39, 5.23)	(4.18, 5.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-0.80, 0.37)
Absolute Change at Week 24 (MMRM)		
n	80	82
LS mean (SE)	0.22 (0.15)	0.02 (0.14)
95% CI of LS mean	(-0.07, 0.51)	(-0.27, 0.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.21 (-0.61, 0.20)
Week 52		
n	76	86
Mean (SD)	4.74 (1.85)	4.59 (1.92)
Absolute Change at Week 52		
n	75	82
Mean (SD)	0.03 (1.63)	-0.07 (1.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52 (MMRM)		
n	75	86
LS mean (SE)	4.68 (0.21)	4.56 (0.20)
95% CI of LS mean	(4.26, 5.10)	(4.17, 4.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.12 (-0.69, 0.46)
Absolute Change at Week 52 (MMRM)		
n	74	82
LS mean (SE)	0.07 (0.19)	-0.06 (0.19)
95% CI of LS mean	(-0.32, 0.45)	(-0.43, 0.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-0.66, 0.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	81	85
LS mean (SE)	0.15 (0.15)	-0.02 (0.14)
95% CI of LS mean	(-0.14, 0.43)	(-0.30, 0.26)
P-value within Treatment	0.3186	0.8663
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-0.57, 0.23)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4049
Hedges' G (SE)		-0.13 (0.15)
Hedges' 95% CI		(-0.43, 0.18)
Hedges' P-value		0.4049

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	30	25
Mean (SD)	4.87 (1.68)	4.60 (1.61)
Week 4 (MMRM)		
n	29	25
LS mean (SE)	4.75 (0.32)	4.54 (0.35)
95% CI of LS mean	(4.10, 5.39)	(3.84, 5.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.21 (-1.17, 0.75)
Absolute Change at Week 4 (MMRM)		
n	28	24
LS mean (SE)	-0.04 (0.24)	-0.28 (0.26)
95% CI of LS mean	(-0.53, 0.45)	(-0.81, 0.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-0.96, 0.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 24 (MMRM)		
n	28	23
LS mean (SE)	4.79 (0.31)	4.50 (0.34)
95% CI of LS mean	(4.16, 5.41)	(3.82, 5.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.29 (-1.22, 0.64)
Absolute Change at Week 24 (MMRM)		
n	27	22
LS mean (SE)	-0.05 (0.30)	-0.18 (0.33)
95% CI of LS mean	(-0.65, 0.56)	(-0.85, 0.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-1.04, 0.77)
Week 52		
n	27	24
Mean (SD)	4.93 (2.15)	4.17 (1.74)
Absolute Change at Week 52		
n	26	23
Mean (SD)	0.19 (1.98)	-0.48 (1.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52 (MMRM)		
n	27	23
LS mean (SE)	4.94 (0.38)	4.20 (0.41)
95% CI of LS mean	(4.18, 5.69)	(3.37, 5.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.74 (-1.86, 0.38)
Absolute Change at Week 52 (MMRM)		
n	26	22
LS mean (SE)	0.13 (0.36)	-0.49 (0.39)
95% CI of LS mean	(-0.60, 0.86)	(-1.28, 0.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.62 (-1.70, 0.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	27	23
LS mean (SE)	0.04 (0.29)	-0.33 (0.32)
95% CI of LS mean	(-0.54, 0.62)	(-0.97, 0.30)
P-value within Treatment	0.8871	0.2965
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-1.24, 0.49)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3874
Hedges' G (SE)		-0.24 (0.28)
Hedges' 95% CI		(-0.81, 0.32)
Hedges' P-value		0.3877

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	166	165
Mean (SD)	5.10 (2.33)	5.03 (2.17)
Week 4 (MMRM)		
n	162	164
LS mean (SE)	4.96 (0.16)	4.85 (0.16)
95% CI of LS mean	(4.65, 5.27)	(4.54, 5.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-0.54, 0.34)
Absolute Change at Week 4 (MMRM)		
n	157	159
LS mean (SE)	-0.09 (0.12)	-0.16 (0.12)
95% CI of LS mean	(-0.32, 0.13)	(-0.39, 0.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-0.39, 0.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 24 (MMRM)		
n	165	155
LS mean (SE)	5.10 (0.18)	4.99 (0.18)
95% CI of LS mean	(4.76, 5.45)	(4.64, 5.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-0.60, 0.38)
Absolute Change at Week 24 (MMRM)		
n	161	152
LS mean (SE)	0.04 (0.13)	-0.03 (0.13)
95% CI of LS mean	(-0.21, 0.29)	(-0.28, 0.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-0.42, 0.29)
Week 52		
n	161	157
Mean (SD)	4.96 (2.02)	4.92 (2.06)
Absolute Change at Week 52		
n	156	152
Mean (SD)	-0.17 (1.61)	-0.20 (1.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52 (MMRM)		
n	159	155
LS mean (SE)	4.94 (0.16)	4.91 (0.16)
95% CI of LS mean	(4.63, 5.25)	(4.59, 5.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-0.47, 0.40)
Absolute Change at Week 52 (MMRM)		
n	154	150
LS mean (SE)	-0.15 (0.14)	-0.16 (0.15)
95% CI of LS mean	(-0.43, 0.14)	(-0.45, 0.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.01 (-0.42, 0.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	162	156
LS mean (SE)	-0.05 (0.12)	-0.09 (0.12)
95% CI of LS mean	(-0.29, 0.18)	(-0.33, 0.14)
P-value within Treatment	0.6550	0.4363
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-0.37, 0.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8094
Hedges' G (SE)		-0.03 (0.11)
Hedges' 95% CI		(-0.25, 0.19)
Hedges' P-value		0.8093

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	17	17
Mean (SD)	4.53 (1.97)	5.71 (2.71)
Week 4 (MMRM)		
n	18	16
LS mean (SE)	4.72 (0.55)	5.04 (0.59)
95% CI of LS mean	(3.61, 5.84)	(3.84, 6.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.32 (-1.34, 1.98)
Absolute Change at Week 4 (MMRM)		
n	16	16
LS mean (SE)	0.04 (0.49)	-0.83 (0.50)
95% CI of LS mean	(-0.96, 1.04)	(-1.85, 0.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.87 (-2.31, 0.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 24 (MMRM)		
n	18	15
LS mean (SE)	5.11 (0.54)	5.40 (0.59)
95% CI of LS mean	(4.00, 6.22)	(4.19, 6.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.29 (-1.37, 1.95)
Absolute Change at Week 24 (MMRM)		
n	17	15
LS mean (SE)	0.49 (0.47)	-0.48 (0.50)
95% CI of LS mean	(-0.48, 1.46)	(-1.50, 0.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.97 (-2.39, 0.46)
Week 52		
n	17	13
Mean (SD)	4.76 (1.92)	5.54 (2.03)
Absolute Change at Week 52		
n	15	13
Mean (SD)	0.20 (1.15)	-0.54 (1.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52 (MMRM)		
n	17	13
LS mean (SE)	4.69 (0.45)	5.42 (0.51)
95% CI of LS mean	(3.77, 5.61)	(4.39, 6.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.73 (-0.68, 2.14)
Absolute Change at Week 52 (MMRM)		
n	15	13
LS mean (SE)	0.21 (0.41)	-0.64 (0.43)
95% CI of LS mean	(-0.62, 1.05)	(-1.53, 0.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.86 (-2.10, 0.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	17	16
LS mean (SE)	0.35 (0.37)	-0.56 (0.39)
95% CI of LS mean	(-0.41, 1.12)	(-1.36, 0.24)
P-value within Treatment	0.3507	0.1610
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.91 (-2.04, 0.21)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1079
Hedges' G (SE)		-0.58 (0.35)
Hedges' 95% CI		(-1.28, 0.13)
Hedges' P-value		0.1066

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	178	171
Mean (SD)	5.12 (2.27)	4.89 (2.04)
Week 4 (MMRM)		
n	173	173
LS mean (SE)	4.94 (0.15)	4.80 (0.15)
95% CI of LS mean	(4.65, 5.23)	(4.50, 5.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-0.56, 0.27)
Absolute Change at Week 4 (MMRM)		
n	169	167
LS mean (SE)	-0.10 (0.10)	-0.12 (0.11)
95% CI of LS mean	(-0.30, 0.11)	(-0.33, 0.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.02 (-0.32, 0.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 24 (MMRM)		
n	175	163
LS mean (SE)	5.04 (0.16)	4.89 (0.17)
95% CI of LS mean	(4.72, 5.37)	(4.56, 5.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.16 (-0.62, 0.31)
Absolute Change at Week 24 (MMRM)		
n	171	159
LS mean (SE)	-0.01 (0.12)	-0.02 (0.12)
95% CI of LS mean	(-0.25, 0.22)	(-0.26, 0.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-0.34, 0.33)
Week 52		
n	170	167
Mean (SD)	4.98 (2.06)	4.75 (2.03)
Absolute Change at Week 52		
n	166	161
Mean (SD)	-0.15 (1.70)	-0.21 (1.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52 (MMRM)		
n	169	165
LS mean (SE)	4.96 (0.15)	4.77 (0.16)
95% CI of LS mean	(4.65, 5.26)	(4.46, 5.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.19 (-0.62, 0.24)
Absolute Change at Week 52 (MMRM)		
n	165	159
LS mean (SE)	-0.12 (0.14)	-0.17 (0.14)
95% CI of LS mean	(-0.40, 0.16)	(-0.46, 0.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-0.45, 0.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	172	163
LS mean (SE)	-0.07 (0.11)	-0.09 (0.12)
95% CI of LS mean	(-0.29, 0.16)	(-0.32, 0.14)
P-value within Treatment	0.5602	0.4231
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-0.35, 0.30)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8680
Hedges' G (SE)		-0.02 (0.11)
Hedges' 95% CI		(-0.23, 0.20)
Hedges' P-value		0.8679

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	115	113
Mean (SD)	4.91 (2.33)	4.74 (1.92)
Week 4 (MMRM)		
n	112	114
LS mean (SE)	4.65 (0.18)	4.67 (0.18)
95% CI of LS mean	(4.29, 5.02)	(4.31, 5.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-0.50, 0.53)
Absolute Change at Week 4 (MMRM)		
n	108	111
LS mean (SE)	-0.15 (0.13)	-0.07 (0.13)
95% CI of LS mean	(-0.40, 0.10)	(-0.32, 0.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.09 (-0.27, 0.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 24 (MMRM)		
n	115	108
LS mean (SE)	4.90 (0.20)	4.73 (0.20)
95% CI of LS mean	(4.51, 5.29)	(4.33, 5.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-0.73, 0.39)
Absolute Change at Week 24 (MMRM)		
n	111	106
LS mean (SE)	0.07 (0.14)	0.00 (0.14)
95% CI of LS mean	(-0.21, 0.34)	(-0.28, 0.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-0.46, 0.33)
Week 52		
n	112	110
Mean (SD)	4.85 (2.06)	4.94 (2.23)
Absolute Change at Week 52		
n	108	107
Mean (SD)	-0.06 (1.65)	0.11 (1.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52 (MMRM)		
n	111	110
LS mean (SE)	4.84 (0.20)	4.90 (0.20)
95% CI of LS mean	(4.46, 5.23)	(4.52, 5.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.06 (-0.49, 0.61)
Absolute Change at Week 52 (MMRM)		
n	107	107
LS mean (SE)	-0.02 (0.16)	0.12 (0.16)
95% CI of LS mean	(-0.33, 0.30)	(-0.19, 0.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-0.31, 0.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	111
LS mean (SE)	0.02 (0.14)	0.06 (0.14)
95% CI of LS mean	(-0.24, 0.29)	(-0.20, 0.33)
P-value within Treatment	0.8538	0.6402
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.04 (-0.34, 0.42)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8413
Hedges' G (SE)		0.03 (0.13)
Hedges' 95% CI		(-0.24, 0.29)
Hedges' P-value		0.8408

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	81	77
Mean (SD)	5.27 (2.10)	5.31 (2.32)
Week 4 (MMRM)		
n	79	75
LS mean (SE)	5.29 (0.22)	5.06 (0.23)
95% CI of LS mean	(4.85, 5.74)	(4.60, 5.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-0.87, 0.41)
Absolute Change at Week 4 (MMRM)		
n	77	72
LS mean (SE)	-0.01 (0.18)	-0.33 (0.19)
95% CI of LS mean	(-0.36, 0.35)	(-0.70, 0.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.32 (-0.83, 0.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 24 (MMRM)		
n	78	70
LS mean (SE)	5.24 (0.25)	5.26 (0.27)
95% CI of LS mean	(4.74, 5.74)	(4.73, 5.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-0.71, 0.74)
Absolute Change at Week 24 (MMRM)		
n	77	68
LS mean (SE)	-0.05 (0.20)	-0.10 (0.21)
95% CI of LS mean	(-0.44, 0.34)	(-0.51, 0.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-0.62, 0.53)
Week 52		
n	76	71
Mean (SD)	5.12 (2.00)	4.63 (1.69)
Absolute Change at Week 52		
n	74	68
Mean (SD)	-0.20 (1.70)	-0.79 (2.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52 (MMRM)		
n	75	68
LS mean (SE)	5.06 (0.21)	4.67 (0.22)
95% CI of LS mean	(4.63, 5.48)	(4.23, 5.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-1.00, 0.23)
Absolute Change at Week 52 (MMRM)		
n	73	65
LS mean (SE)	-0.24 (0.23)	-0.72 (0.24)
95% CI of LS mean	(-0.69, 0.21)	(-1.20, -0.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.48 (-1.14, 0.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	78	68
LS mean (SE)	-0.15 (0.18)	-0.41 (0.19)
95% CI of LS mean	(-0.51, 0.22)	(-0.79, -0.03)
P-value within Treatment	0.4261	0.0363
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-0.79, 0.26)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3241
Hedges' G (SE)		-0.16 (0.17)
Hedges' 95% CI		(-0.49, 0.16)
Hedges' P-value		0.3244

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	4.84 (1.89)	4.95 (1.92)
Week 4 (MMRM)		
n	85	84
LS mean (SE)	4.94 (0.22)	4.87 (0.22)
95% CI of LS mean	(4.50, 5.37)	(4.43, 5.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-0.69, 0.55)
Absolute Change at Week 4 (MMRM)		
n	82	82
LS mean (SE)	0.04 (0.14)	-0.09 (0.14)
95% CI of LS mean	(-0.23, 0.32)	(-0.37, 0.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-0.52, 0.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 24 (MMRM)		
n	88	82
LS mean (SE)	5.02 (0.24)	5.09 (0.25)
95% CI of LS mean	(4.54, 5.50)	(4.60, 5.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-0.61, 0.75)
Absolute Change at Week 24 (MMRM)		
n	86	80
LS mean (SE)	0.14 (0.16)	0.18 (0.16)
95% CI of LS mean	(-0.17, 0.45)	(-0.13, 0.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.04 (-0.40, 0.48)
Week 52		
n	85	78
Mean (SD)	4.88 (1.96)	5.08 (2.19)
Absolute Change at Week 52		
n	82	76
Mean (SD)	-0.07 (1.55)	0.04 (1.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52 (MMRM)		
n	84	77
LS mean (SE)	4.83 (0.22)	5.05 (0.23)
95% CI of LS mean	(4.39, 5.26)	(4.60, 5.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.22 (-0.40, 0.85)
Absolute Change at Week 52 (MMRM)		
n	81	75
LS mean (SE)	-0.09 (0.18)	0.08 (0.18)
95% CI of LS mean	(-0.44, 0.26)	(-0.28, 0.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-0.33, 0.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	86	80
LS mean (SE)	0.03 (0.13)	0.13 (0.14)
95% CI of LS mean	(-0.24, 0.29)	(-0.14, 0.41)
P-value within Treatment	0.8378	0.3392
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.11 (-0.28, 0.49)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5861
Hedges' G (SE)		0.08 (0.15)
Hedges' 95% CI		(-0.22, 0.39)
Hedges' P-value		0.5859

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	108	105
Mean (SD)	5.24 (2.48)	4.99 (2.25)
Week 4 (MMRM)		
n	106	105
LS mean (SE)	4.91 (0.19)	4.77 (0.19)
95% CI of LS mean	(4.54, 5.28)	(4.40, 5.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-0.67, 0.39)
Absolute Change at Week 4 (MMRM)		
n	103	101
LS mean (SE)	-0.19 (0.15)	-0.24 (0.15)
95% CI of LS mean	(-0.49, 0.11)	(-0.55, 0.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-0.48, 0.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 24 (MMRM)		
n	105	96
LS mean (SE)	5.07 (0.21)	4.81 (0.21)
95% CI of LS mean	(4.66, 5.48)	(4.39, 5.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-0.84, 0.33)
Absolute Change at Week 24 (MMRM)		
n	102	94
LS mean (SE)	-0.07 (0.17)	-0.22 (0.17)
95% CI of LS mean	(-0.40, 0.26)	(-0.56, 0.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-0.62, 0.33)
Week 52		
n	103	103
Mean (SD)	5.02 (2.10)	4.62 (1.89)
Absolute Change at Week 52		
n	100	99
Mean (SD)	-0.15 (1.76)	-0.45 (2.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52 (MMRM)		
n	102	101
LS mean (SE)	5.04 (0.19)	4.63 (0.20)
95% CI of LS mean	(4.66, 5.42)	(4.25, 5.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.40 (-0.95, 0.14)
Absolute Change at Week 52 (MMRM)		
n	99	97
LS mean (SE)	-0.11 (0.20)	-0.43 (0.20)
95% CI of LS mean	(-0.50, 0.27)	(-0.82, -0.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-0.86, 0.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.13.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	103	99
LS mean (SE)	-0.09 (0.17)	-0.32 (0.17)
95% CI of LS mean	(-0.42, 0.23)	(-0.66, 0.01)
P-value within Treatment	0.5738	0.0584
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-0.70, 0.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3355
Hedges' G (SE)		-0.14 (0.14)
Hedges' 95% CI		(-0.41, 0.14)
Hedges' P-value		0.3360

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with any TEAEs	191 (94.55)	183 (93.37)
Relative Risk (RR) (95% CI)		0.9874 (0.9394, 1.0379)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6195
Odds Ratio (OR) (95% CI)		0.8107 (0.3542, 1.8558)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6195
Risk Difference (RD) (95% CI)		-0.0119 (-0.0587, 0.0350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6193
Infections and infestations	143 (70.79)	129 (65.82)
Relative Risk (RR) (95% CI)		0.9297 (0.8129, 1.0633)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2874
Odds Ratio (OR) (95% CI)		0.7944 (0.5203, 1.2129)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2864
Risk Difference (RD) (95% CI)		-0.0498 (-0.1411, 0.0416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2856

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
COVID-19	54 (26.73)	49 (25.00)
Relative Risk (RR) (95% CI)		0.9352 (0.6703, 1.3048)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6933
Odds Ratio (OR) (95% CI)		0.9136 (0.5831, 1.4314)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6932
Risk Difference (RD) (95% CI)		-0.0173 (-0.1033, 0.0687)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6930
Nasopharyngitis	35 (17.33)	45 (22.96)
Relative Risk (RR) (95% CI)		1.3251 (0.8921, 1.9681)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1632
Odds Ratio (OR) (95% CI)		1.4219 (0.8681, 2.3293)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1621

- MedDRA version 26.1.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0563 (-0.0224, 0.1350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1606

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Influenza	10 (4.95)	19 (9.69)
Relative Risk (RR) (95% CI)		1.9582 (0.9342, 4.1045)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0751
Odds Ratio (OR) (95% CI)		2.0610 (0.9331, 4.5526)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0737
Risk Difference (RD) (95% CI)		0.0474 (-0.0037, 0.0985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0688
Upper respiratory tract infection	27 (13.37)	17 (8.67)
Relative Risk (RR) (95% CI)		0.6489 (0.3655, 1.1522)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1398
Odds Ratio (OR) (95% CI)		0.6156 (0.3241, 1.1693)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1383

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0469 (-0.1082, 0.0143)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1333

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Viral upper respiratory tract infection	18 (8.91)	17 (8.67)
Relative Risk (RR) (95% CI)		0.9734 (0.5168, 1.8332)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9334
Odds Ratio (OR) (95% CI)		0.9708 (0.4850, 1.9434)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9334
Risk Difference (RD) (95% CI)		-0.0024 (-0.0580, 0.0533)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9334
Sinusitis	10 (4.95)	10 (5.10)
Relative Risk (RR) (95% CI)		1.0306 (0.4386, 2.4214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9448
Odds Ratio (OR) (95% CI)		1.0323 (0.4199, 2.5375)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9448

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0015 (-0.0414, 0.0445)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9449

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Respiratory tract infection	12 (5.94)	8 (4.08)
Relative Risk (RR) (95% CI)		0.6871 (0.2871, 1.6445)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3993
Odds Ratio (OR) (95% CI)		0.6738 (0.2693, 1.6857)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3987
Risk Difference (RD) (95% CI)		-0.0186 (-0.0614, 0.0242)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3944
Rhinitis	6 (2.97)	8 (4.08)
Relative Risk (RR) (95% CI)		1.3741 (0.4857, 3.8882)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5492
Odds Ratio (OR) (95% CI)		1.3901 (0.4734, 4.0821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5490

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0111 (-0.0252, 0.0474)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5481

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Oral candidiasis	6 (2.97)	4 (2.04)
Relative Risk (RR) (95% CI)		0.6871 (0.1969, 2.3976)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5561
Odds Ratio (OR) (95% CI)		0.6806 (0.1891, 2.4494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5559
Risk Difference (RD) (95% CI)		-0.0093 (-0.0400, 0.0214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5524
Respiratory, thoracic and mediastinal disorders	98 (48.51)	94 (47.96)
Relative Risk (RR) (95% CI)		0.9885 (0.8065, 1.2118)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9117
Odds Ratio (OR) (95% CI)		0.9780 (0.6600, 1.4492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9117
Risk Difference (RD) (95% CI)		-0.0056 (-0.1037, 0.0926)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9117

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Cough	41 (20.30)	45 (22.96)
Relative Risk (RR) (95% CI)		1.1312 (0.7776, 1.6454)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5192
Odds Ratio (OR) (95% CI)		1.1702 (0.7257, 1.8872)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5191
Risk Difference (RD) (95% CI)		0.0266 (-0.0543, 0.1075)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5189
Oropharyngeal pain	23 (11.39)	24 (12.24)
Relative Risk (RR) (95% CI)		1.0754 (0.6285, 1.8401)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7907
Odds Ratio (OR) (95% CI)		1.0859 (0.5906, 1.9966)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7907

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0086 (-0.0549, 0.0720)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7908

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Nasal congestion	24 (11.88)	19 (9.69)
Relative Risk (RR) (95% CI)		0.8159 (0.4619, 1.4411)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4833
Odds Ratio (OR) (95% CI)		0.7961 (0.4211, 1.5051)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4829
Risk Difference (RD) (95% CI)		-0.0219 (-0.0828, 0.0390)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4813
Rhinorrhoea	14 (6.93)	19 (9.69)
Relative Risk (RR) (95% CI)		1.3987 (0.7216, 2.7110)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3204
Odds Ratio (OR) (95% CI)		1.4415 (0.7015, 2.9621)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3197

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0276 (-0.0266, 0.0819)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3181

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Sputum increased	21 (10.40)	18 (9.18)
Relative Risk (RR) (95% CI)		0.8834 (0.4857, 1.6066)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6845
Odds Ratio (OR) (95% CI)		0.8716 (0.4493, 1.6909)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6844
Risk Difference (RD) (95% CI)		-0.0121 (-0.0705, 0.0462)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6839
Sinus congestion	5 (2.48)	14 (7.14)
Relative Risk (RR) (95% CI)		2.8857 (1.0594, 7.8601)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0382
Odds Ratio (OR) (95% CI)		3.0308 (1.0704, 8.5817)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0368

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0467 (0.0047, 0.0886)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0292

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Haemoptysis	11 (5.45)	13 (6.63)
Relative Risk (RR) (95% CI)		1.2180 (0.5592, 2.6531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6196
Odds Ratio (OR) (95% CI)		1.2335 (0.5389, 2.8235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6195
Risk Difference (RD) (95% CI)		0.0119 (-0.0350, 0.0587)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6193
Productive cough	5 (2.48)	12 (6.12)
Relative Risk (RR) (95% CI)		2.4735 (0.8878, 6.8910)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0832
Odds Ratio (OR) (95% CI)		2.5696 (0.8881, 7.4349)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0817

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
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Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0365 (-0.0033, 0.0763)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0726

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Respiration abnormal	5 (2.48)	8 (4.08)
Relative Risk (RR) (95% CI)		1.6490 (0.5489, 4.9535)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3728
Odds Ratio (OR) (95% CI)		1.6766 (0.5389, 5.2166)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3722
Risk Difference (RD) (95% CI)		0.0161 (-0.0190, 0.0511)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3686
Dyspnoea	7 (3.47)	7 (3.57)
Relative Risk (RR) (95% CI)		1.0306 (0.3683, 2.8841)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9542
Odds Ratio (OR) (95% CI)		1.0317 (0.3551, 2.9977)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9542

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Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0011 (-0.0351, 0.0373)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9542

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Sputum discoloured	6 (2.97)	4 (2.04)
Relative Risk (RR) (95% CI)		0.6871 (0.1969, 2.3976)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5561
Odds Ratio (OR) (95% CI)		0.6806 (0.1891, 2.4494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5559
Risk Difference (RD) (95% CI)		-0.0093 (-0.0400, 0.0214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5524
Investigations	72 (35.64)	72 (36.73)
Relative Risk (RR) (95% CI)		1.0306 (0.7939, 1.3379)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8208
Odds Ratio (OR) (95% CI)		1.0484 (0.6965, 1.5781)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8208
Risk Difference (RD) (95% CI)		0.0109 (-0.0835, 0.1053)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8208

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Blood creatine phosphokinase increased	24 (11.88)	18 (9.18)
Relative Risk (RR) (95% CI)		0.7730 (0.4334, 1.3787)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3831
Odds Ratio (OR) (95% CI)		0.7500 (0.3933, 1.4302)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3824
Risk Difference (RD) (95% CI)		-0.0270 (-0.0872, 0.0332)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3799
Alanine aminotransferase increased	11 (5.45)	13 (6.63)
Relative Risk (RR) (95% CI)		1.2180 (0.5592, 2.6531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6196
Odds Ratio (OR) (95% CI)		1.2335 (0.5389, 2.8235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6195

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0119 (-0.0350, 0.0587)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6193

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Aspartate aminotransferase increased	9 (4.46)	12 (6.12)
Relative Risk (RR) (95% CI)		1.3741 (0.5923, 3.1882)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4592
Odds Ratio (OR) (95% CI)		1.3986 (0.5757, 3.3973)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4588
Risk Difference (RD) (95% CI)		0.0167 (-0.0273, 0.0607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4578
Weight decreased	1 (0.50)	9 (4.59)
Relative Risk (RR) (95% CI)		9.2755 (1.1862, 72.5295)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0338
Odds Ratio (OR) (95% CI)		9.6738 (1.2139, 77.0904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0321

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Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0410 (0.0101, 0.0718)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0093

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
SARS-CoV-2 test positive	3 (1.49)	8 (4.08)
Relative Risk (RR) (95% CI)		2.7483 (0.7399, 10.2088)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1311
Odds Ratio (OR) (95% CI)		2.8227 (0.7378, 10.7993)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1296
Risk Difference (RD) (95% CI)		0.0260 (-0.0064, 0.0583)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1155
Bacterial test positive	6 (2.97)	7 (3.57)
Relative Risk (RR) (95% CI)		1.2024 (0.4114, 3.5144)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7363
Odds Ratio (OR) (95% CI)		1.2099 (0.3993, 3.6660)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7362

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0060 (-0.0290, 0.0410)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7362

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Blood bilirubin increased	7 (3.47)	4 (2.04)
Relative Risk (RR) (95% CI)		0.5889 (0.1751, 1.9802)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3921
Odds Ratio (OR) (95% CI)		0.5804 (0.1672, 2.0146)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3915
Risk Difference (RD) (95% CI)		-0.0142 (-0.0463, 0.0178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3839
Gastrointestinal disorders	68 (33.66)	64 (32.65)
Relative Risk (RR) (95% CI)		0.9700 (0.7338, 1.2823)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8306
Odds Ratio (OR) (95% CI)		0.9554 (0.6294, 1.4505)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8305
Risk Difference (RD) (95% CI)		-0.0101 (-0.1026, 0.0824)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8305

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Diarrhoea	15 (7.43)	21 (10.71)
Relative Risk (RR) (95% CI)		1.4429 (0.7663, 2.7167)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2561
Odds Ratio (OR) (95% CI)		1.4960 (0.7474, 2.9943)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2552
Risk Difference (RD) (95% CI)		0.0329 (-0.0235, 0.0893)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2532
Abdominal pain upper	6 (2.97)	12 (6.12)
Relative Risk (RR) (95% CI)		2.0612 (0.7892, 5.3837)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1398
Odds Ratio (OR) (95% CI)		2.1304 (0.7834, 5.7936)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1384

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0315 (-0.0094, 0.0724)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1311

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Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Abdominal pain	14 (6.93)	10 (5.10)
Relative Risk (RR) (95% CI)		0.7362 (0.3350, 1.6177)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4457
Odds Ratio (OR) (95% CI)		0.7220 (0.3128, 1.6664)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4452
Risk Difference (RD) (95% CI)		-0.0183 (-0.0649, 0.0284)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4422
Constipation	10 (4.95)	7 (3.57)
Relative Risk (RR) (95% CI)		0.7214 (0.2802, 1.8574)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4986
Odds Ratio (OR) (95% CI)		0.7111 (0.2651, 1.9072)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4982

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0138 (-0.0534, 0.0258)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4951

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Nausea	17 (8.42)	7 (3.57)
Relative Risk (RR) (95% CI)		0.4244 (0.1799, 1.0008)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0502
Odds Ratio (OR) (95% CI)		0.4031 (0.1633, 0.9946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0486
Risk Difference (RD) (95% CI)		-0.0484 (-0.0947, -0.0022)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0402
Flatulence	7 (3.47)	6 (3.06)
Relative Risk (RR) (95% CI)		0.8834 (0.3022, 2.5820)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8207
Odds Ratio (OR) (95% CI)		0.8797 (0.2903, 2.6655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8207

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Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0040 (-0.0389, 0.0309)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8204

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Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Abdominal distension	10 (4.95)	5 (2.55)
Relative Risk (RR) (95% CI)		0.5153 (0.1794, 1.4805)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2182
Odds Ratio (OR) (95% CI)		0.5026 (0.1686, 1.4980)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2170
Risk Difference (RD) (95% CI)		-0.0240 (-0.0612, 0.0132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2059
Vomiting	8 (3.96)	3 (1.53)
Relative Risk (RR) (95% CI)		0.3865 (0.1040, 1.4356)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1556
Odds Ratio (OR) (95% CI)		0.3769 (0.0985, 1.4421)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1541

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0243 (-0.0562, 0.0076)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1357

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
General disorders and administration site conditions	47 (23.27)	56 (28.57)
Relative Risk (RR) (95% CI)		1.2280 (0.8791, 1.7153)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2285
Odds Ratio (OR) (95% CI)		1.3191 (0.8411, 2.0690)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2277
Risk Difference (RD) (95% CI)		0.0530 (-0.0330, 0.1390)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2267
Pyrexia	21 (10.40)	24 (12.24)
Relative Risk (RR) (95% CI)		1.1778 (0.6784, 2.0450)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		1.2027 (0.6458, 2.2395)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607
Risk Difference (RD) (95% CI)		0.0185 (-0.0438, 0.0808)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5606

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Fatigue	16 (7.92)	18 (9.18)
Relative Risk (RR) (95% CI)		1.1594 (0.6089, 2.2079)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6526
Odds Ratio (OR) (95% CI)		1.1756 (0.5814, 2.3770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6525
Risk Difference (RD) (95% CI)		0.0126 (-0.0423, 0.0676)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6525
Pain	6 (2.97)	8 (4.08)
Relative Risk (RR) (95% CI)		1.3741 (0.4857, 3.8882)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5492
Odds Ratio (OR) (95% CI)		1.3901 (0.4734, 4.0821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5490

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0111 (-0.0252, 0.0474)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5481

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Musculoskeletal and connective tissue disorders	48 (23.76)	41 (20.92)
Relative Risk (RR) (95% CI)		0.8803 (0.6095, 1.2714)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4967
Odds Ratio (OR) (95% CI)		0.8487 (0.5290, 1.3615)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4962
Risk Difference (RD) (95% CI)		-0.0284 (-0.1102, 0.0533)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4955
Arthralgia	11 (5.45)	10 (5.10)
Relative Risk (RR) (95% CI)		0.9369 (0.4071, 2.1562)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8782
Odds Ratio (OR) (95% CI)		0.9335 (0.3873, 2.2503)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8782
Risk Difference (RD) (95% CI)		-0.0034 (-0.0473, 0.0405)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8781

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Back pain	16 (7.92)	9 (4.59)
Relative Risk (RR) (95% CI)		0.5797 (0.2624, 1.2807)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1776
Odds Ratio (OR) (95% CI)		0.5595 (0.2412, 1.2979)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1762
Risk Difference (RD) (95% CI)		-0.0333 (-0.0807, 0.0141)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1686
Myalgia	3 (1.49)	7 (3.57)
Relative Risk (RR) (95% CI)		2.4048 (0.6308, 9.1669)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1987
Odds Ratio (OR) (95% CI)		2.4568 (0.6261, 9.6401)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1975

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0209 (-0.0100, 0.0517)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1854

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Nervous system disorders	34 (16.83)	39 (19.90)
Relative Risk (RR) (95% CI)		1.1822 (0.7800, 1.7916)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4302
Odds Ratio (OR) (95% CI)		1.2274 (0.7380, 2.0414)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4298
Risk Difference (RD) (95% CI)		0.0307 (-0.0454, 0.1067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4295
Headache	22 (10.89)	25 (12.76)
Relative Risk (RR) (95% CI)		1.1712 (0.6837, 2.0061)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5651
Odds Ratio (OR) (95% CI)		1.1962 (0.6500, 2.2014)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5649
Risk Difference (RD) (95% CI)		0.0186 (-0.0448, 0.0821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5648

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Injury, poisoning and procedural complications	36 (17.82)	36 (18.37)
Relative Risk (RR) (95% CI)		1.0306 (0.6785, 1.5656)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8876
Odds Ratio (OR) (95% CI)		1.0375 (0.6227, 1.7285)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8876
Risk Difference (RD) (95% CI)		0.0055 (-0.0702, 0.0811)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8876
Skin and subcutaneous tissue disorders	35 (17.33)	30 (15.31)
Relative Risk (RR) (95% CI)		0.8834 (0.5654, 1.3803)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5861
Odds Ratio (OR) (95% CI)		0.8623 (0.5061, 1.4692)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5858
Risk Difference (RD) (95% CI)		-0.0202 (-0.0928, 0.0524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5852

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Rash	9 (4.46)	12 (6.12)
Relative Risk (RR) (95% CI)		1.3741 (0.5923, 3.1882)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4592
Odds Ratio (OR) (95% CI)		1.3986 (0.5757, 3.3973)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4588
Risk Difference (RD) (95% CI)		0.0167 (-0.0273, 0.0607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4578
Acne	8 (3.96)	5 (2.55)
Relative Risk (RR) (95% CI)		0.6441 (0.2144, 1.9350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4332
Odds Ratio (OR) (95% CI)		0.6348 (0.2040, 1.9752)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4327

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0141 (-0.0489, 0.0207)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4272

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Metabolism and nutrition disorders	18 (8.91)	20 (10.20)
Relative Risk (RR) (95% CI)		1.1451 (0.6249, 2.0985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6610
Odds Ratio (OR) (95% CI)		1.1616 (0.5947, 2.2689)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6610
Risk Difference (RD) (95% CI)		0.0129 (-0.0449, 0.0707)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6609
Hypoglycaemia	7 (3.47)	5 (2.55)
Relative Risk (RR) (95% CI)		0.7362 (0.2376, 2.2804)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5954
Odds Ratio (OR) (95% CI)		0.7292 (0.2275, 2.3376)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5952
Risk Difference (RD) (95% CI)		-0.0091 (-0.0427, 0.0244)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5929

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Psychiatric disorders	34 (16.83)	19 (9.69)
Relative Risk (RR) (95% CI)		0.5759 (0.3404, 0.9744)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0397
Odds Ratio (OR) (95% CI)		0.5304 (0.2912, 0.9663)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0383
Risk Difference (RD) (95% CI)		-0.0714 (-0.1375, -0.0052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0345
Depression	7 (3.47)	4 (2.04)
Relative Risk (RR) (95% CI)		0.5889 (0.1751, 1.9802)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3921
Odds Ratio (OR) (95% CI)		0.5804 (0.1672, 2.0146)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3915
Risk Difference (RD) (95% CI)		-0.0142 (-0.0463, 0.0178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3839

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Insomnia	8 (3.96)	4 (2.04)
Relative Risk (RR) (95% CI)		0.5153 (0.1577, 1.6838)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2724
Odds Ratio (OR) (95% CI)		0.5052 (0.1496, 1.7056)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2714
Risk Difference (RD) (95% CI)		-0.0192 (-0.0526, 0.0142)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2599
Immune system disorders	2 (0.99)	8 (4.08)
Relative Risk (RR) (95% CI)		4.1224 (0.8865, 19.1715)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0709
Odds Ratio (OR) (95% CI)		4.2553 (0.8922, 20.2954)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0692
Risk Difference (RD) (95% CI)		0.0309 (0.0000, 0.0618)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0498

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Eye disorders	9 (4.46)	7 (3.57)
Relative Risk (RR) (95% CI)		0.8016 (0.3045, 2.1103)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6543
Odds Ratio (OR) (95% CI)		0.7942 (0.2899, 2.1761)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6542
Risk Difference (RD) (95% CI)		-0.0088 (-0.0474, 0.0297)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6529
Reproductive system and breast disorders	15 (7.43)	7 (3.57)
Relative Risk (RR) (95% CI)		0.4810 (0.2004, 1.1542)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1012
Odds Ratio (OR) (95% CI)		0.4617 (0.1841, 1.1582)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0996
Risk Difference (RD) (95% CI)		-0.0385 (-0.0831, 0.0060)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0897

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Ear and labyrinth disorders	10 (4.95)	5 (2.55)
Relative Risk (RR) (95% CI)		0.5153 (0.1794, 1.4805)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2182
Odds Ratio (OR) (95% CI)		0.5026 (0.1686, 1.4980)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2170
Risk Difference (RD) (95% CI)		-0.0240 (-0.0612, 0.0132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2059
Renal and urinary disorders	16 (7.92)	5 (2.55)
Relative Risk (RR) (95% CI)		0.3221 (0.1203, 0.8622)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0241
Odds Ratio (OR) (95% CI)		0.3043 (0.1093, 0.8476)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0228
Risk Difference (RD) (95% CI)		-0.0537 (-0.0970, -0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0151

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with any TEAEs	191 (94.55)	183 (93.37)
Relative Risk (RR) (95% CI)		0.9874 (0.9394, 1.0379)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6195
Odds Ratio (OR) (95% CI)		0.8107 (0.3542, 1.8558)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6195
Risk Difference (RD) (95% CI)		-0.0119 (-0.0587, 0.0350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6193
Grade 1/Mild	75 (37.13)	77 (39.29)
Relative Risk (RR) (95% CI)		1.0581 (0.8241, 1.3586)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6579
Odds Ratio (OR) (95% CI)		1.0957 (0.7311, 1.6420)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6579

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0216 (-0.0739, 0.1170)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6579

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	102 (50.50)	88 (44.90)
Relative Risk (RR) (95% CI)		0.8892 (0.7232, 1.0932)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2651
Odds Ratio (OR) (95% CI)		0.7988 (0.5387, 1.1847)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2640
Risk Difference (RD) (95% CI)		-0.0560 (-0.1540, 0.0420)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2629
Grade 3/Severe	14 (6.93)	18 (9.18)
Relative Risk (RR) (95% CI)		1.3251 (0.6779, 2.5901)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4104
Odds Ratio (OR) (95% CI)		1.3579 (0.6558, 2.8119)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4100

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0225 (-0.0310, 0.0760)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4091

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Infections and infestations	143 (70.79)	129 (65.82)
Relative Risk (RR) (95% CI)		0.9297 (0.8129, 1.0633)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2874
Odds Ratio (OR) (95% CI)		0.7944 (0.5203, 1.2129)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2864
Risk Difference (RD) (95% CI)		-0.0498 (-0.1411, 0.0416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2856
Grade 1/Mild	83 (41.09)	69 (35.20)
Relative Risk (RR) (95% CI)		0.8568 (0.6661, 1.1020)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2287
Odds Ratio (OR) (95% CI)		0.7790 (0.5193, 1.1686)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2274

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0589 (-0.1541, 0.0364)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2259

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	57 (28.22)	53 (27.04)
Relative Risk (RR) (95% CI)		0.9583 (0.6971, 1.3173)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7930
Odds Ratio (OR) (95% CI)		0.9428 (0.6075, 1.4633)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7929
Risk Difference (RD) (95% CI)		-0.0118 (-0.0996, 0.0761)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7929
Grade 3/Severe	3 (1.49)	7 (3.57)
Relative Risk (RR) (95% CI)		2.4048 (0.6308, 9.1669)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1987
Odds Ratio (OR) (95% CI)		2.4568 (0.6261, 9.6401)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1975

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
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Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0209 (-0.0100, 0.0517)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1854

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
COVID-19	54 (26.73)	49 (25.00)
Relative Risk (RR) (95% CI)		0.9352 (0.6703, 1.3048)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6933
Odds Ratio (OR) (95% CI)		0.9136 (0.5831, 1.4314)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6932
Risk Difference (RD) (95% CI)		-0.0173 (-0.1033, 0.0687)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6930
Grade 1/Mild	37 (18.32)	34 (17.35)
Relative Risk (RR) (95% CI)		0.9470 (0.6209, 1.4444)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8006
Odds Ratio (OR) (95% CI)		0.9359 (0.5600, 1.5643)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8005

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0097 (-0.0849, 0.0655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8004

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	17 (8.42)	15 (7.65)
Relative Risk (RR) (95% CI)		0.9094 (0.4672, 1.7699)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7798
Odds Ratio (OR) (95% CI)		0.9019 (0.4373, 1.8601)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7797
Risk Difference (RD) (95% CI)		-0.0076 (-0.0610, 0.0458)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7795
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Nasopharyngitis	35 (17.33)	45 (22.96)
Relative Risk (RR) (95% CI)		1.3251 (0.8921, 1.9681)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1632
Odds Ratio (OR) (95% CI)		1.4219 (0.8681, 2.3293)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1621
Risk Difference (RD) (95% CI)		0.0563 (-0.0224, 0.1350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1606
Grade 1/Mild	28 (13.86)	29 (14.80)
Relative Risk (RR) (95% CI)		1.0674 (0.6601, 1.7262)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7902
Odds Ratio (OR) (95% CI)		1.0791 (0.6158, 1.8911)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7902

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0093 (-0.0595, 0.0782)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7902

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	7 (3.47)	16 (8.16)
Relative Risk (RR) (95% CI)		2.3557 (0.9907, 5.6013)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0525
Odds Ratio (OR) (95% CI)		2.4762 (0.9957, 6.1578)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0511
Risk Difference (RD) (95% CI)		0.0470 (0.0011, 0.0929)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0448
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
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Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Influenza	10 (4.95)	19 (9.69)
Relative Risk (RR) (95% CI)		1.9582 (0.9342, 4.1045)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0751
Odds Ratio (OR) (95% CI)		2.0610 (0.9331, 4.5526)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0737
Risk Difference (RD) (95% CI)		0.0474 (-0.0037, 0.0985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0688
Grade 1/Mild	7 (3.47)	6 (3.06)
Relative Risk (RR) (95% CI)		0.8834 (0.3022, 2.5820)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8207
Odds Ratio (OR) (95% CI)		0.8797 (0.2903, 2.6655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8207

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0040 (-0.0389, 0.0309)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8204

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	11 (5.61)
Relative Risk (RR) (95% CI)		5.6684 (1.2727, 25.2460)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0228
Odds Ratio (OR) (95% CI)		5.9459 (1.3007, 27.1820)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0215
Risk Difference (RD) (95% CI)		0.0462 (0.0112, 0.0812)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0096
Grade 3/Severe	1 (0.50)	2 (1.02)
Relative Risk (RR) (95% CI)		2.0612 (0.1884, 22.5492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5535
Odds Ratio (OR) (95% CI)		2.0722 (0.1864, 23.0379)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5533

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0053 (-0.0118, 0.0223)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5465

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Upper respiratory tract infection	27 (13.37)	17 (8.67)
Relative Risk (RR) (95% CI)		0.6489 (0.3655, 1.1522)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1398
Odds Ratio (OR) (95% CI)		0.6156 (0.3241, 1.1693)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1383
Risk Difference (RD) (95% CI)		-0.0469 (-0.1082, 0.0143)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1333
Grade 1/Mild	18 (8.91)	15 (7.65)
Relative Risk (RR) (95% CI)		0.8588 (0.4455, 1.6558)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6496
Odds Ratio (OR) (95% CI)		0.8471 (0.4143, 1.7322)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6494

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0126 (-0.0667, 0.0415)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6487

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	9 (4.46)	2 (1.02)
Relative Risk (RR) (95% CI)		0.2290 (0.0501, 1.0467)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0573
Odds Ratio (OR) (95% CI)		0.2211 (0.0472, 1.0365)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0556
Risk Difference (RD) (95% CI)		-0.0344 (-0.0661, -0.0026)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0339
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Viral upper respiratory tract infection	18 (8.91)	17 (8.67)
Relative Risk (RR) (95% CI)		0.9734 (0.5168, 1.8332)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9334
Odds Ratio (OR) (95% CI)		0.9708 (0.4850, 1.9434)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9334
Risk Difference (RD) (95% CI)		-0.0024 (-0.0580, 0.0533)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9334
Grade 1/Mild	16 (7.92)	13 (6.63)
Relative Risk (RR) (95% CI)		0.8374 (0.4138, 1.6946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6217
Odds Ratio (OR) (95% CI)		0.8258 (0.3863, 1.7654)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6215

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0129 (-0.0639, 0.0381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6206

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	4 (2.04)
Relative Risk (RR) (95% CI)		2.0612 (0.3819, 11.1258)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4004
Odds Ratio (OR) (95% CI)		2.0833 (0.3772, 11.5059)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3999
Risk Difference (RD) (95% CI)		0.0105 (-0.0135, 0.0346)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3918
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Sinusitis	10 (4.95)	10 (5.10)
Relative Risk (RR) (95% CI)		1.0306 (0.4386, 2.4214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9448
Odds Ratio (OR) (95% CI)		1.0323 (0.4199, 2.5375)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9448
Risk Difference (RD) (95% CI)		0.0015 (-0.0414, 0.0445)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9449
Grade 1/Mild	5 (2.48)	6 (3.06)
Relative Risk (RR) (95% CI)		1.2367 (0.3837, 3.9865)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7220
Odds Ratio (OR) (95% CI)		1.2442 (0.3735, 4.1451)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7219

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0059 (-0.0264, 0.0381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7218

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	5 (2.48)	4 (2.04)
Relative Risk (RR) (95% CI)		0.8245 (0.2247, 3.0253)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7711
Odds Ratio (OR) (95% CI)		0.8208 (0.2172, 3.1027)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7710
Risk Difference (RD) (95% CI)		-0.0043 (-0.0335, 0.0248)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7704
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Respiratory tract infection	12 (5.94)	8 (4.08)
Relative Risk (RR) (95% CI)		0.6871 (0.2871, 1.6445)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3993
Odds Ratio (OR) (95% CI)		0.6738 (0.2693, 1.6857)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3987
Risk Difference (RD) (95% CI)		-0.0186 (-0.0614, 0.0242)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3944
Grade 1/Mild	7 (3.47)	5 (2.55)
Relative Risk (RR) (95% CI)		0.7362 (0.2376, 2.2804)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5954
Odds Ratio (OR) (95% CI)		0.7292 (0.2275, 2.3376)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5952

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0091 (-0.0427, 0.0244)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5929

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	5 (2.48)	3 (1.53)
Relative Risk (RR) (95% CI)		0.6184 (0.1498, 2.5526)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5064
Odds Ratio (OR) (95% CI)		0.6124 (0.1444, 2.5980)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5060
Risk Difference (RD) (95% CI)		-0.0094 (-0.0369, 0.0180)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5003
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Rhinitis	6 (2.97)	8 (4.08)
Relative Risk (RR) (95% CI)		1.3741 (0.4857, 3.8882)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5492
Odds Ratio (OR) (95% CI)		1.3901 (0.4734, 4.0821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5490
Risk Difference (RD) (95% CI)		0.0111 (-0.0252, 0.0474)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5481
Grade 1/Mild	4 (1.98)	8 (4.08)
Relative Risk (RR) (95% CI)		2.0612 (0.6308, 6.7351)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2312
Odds Ratio (OR) (95% CI)		2.1064 (0.6239, 7.1113)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2301

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0210 (-0.0127, 0.0547)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2218

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0099 (-0.0236, 0.0038)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1552
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Oral candidiasis	6 (2.97)	4 (2.04)
Relative Risk (RR) (95% CI)		0.6871 (0.1969, 2.3976)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5561
Odds Ratio (OR) (95% CI)		0.6806 (0.1891, 2.4494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5559
Risk Difference (RD) (95% CI)		-0.0093 (-0.0400, 0.0214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5524
Grade 1/Mild	6 (2.97)	3 (1.53)
Relative Risk (RR) (95% CI)		0.5153 (0.1307, 2.0318)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3435
Odds Ratio (OR) (95% CI)		0.5078 (0.1252, 2.0593)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3428

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0144 (-0.0434, 0.0146)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3313

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Respiratory, thoracic and mediastinal disorders	98 (48.51)	94 (47.96)
Relative Risk (RR) (95% CI)		0.9885 (0.8065, 1.2118)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9117
Odds Ratio (OR) (95% CI)		0.9780 (0.6600, 1.4492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9117
Risk Difference (RD) (95% CI)		-0.0056 (-0.1037, 0.0926)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9117
Grade 1/Mild	73 (36.14)	67 (34.18)
Relative Risk (RR) (95% CI)		0.9459 (0.7242, 1.2355)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6832
Odds Ratio (OR) (95% CI)		0.9178 (0.6081, 1.3854)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6831

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0195 (-0.1133, 0.0743)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6829

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	24 (11.88)	22 (11.22)
Relative Risk (RR) (95% CI)		0.9447 (0.5483, 1.6278)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8377
Odds Ratio (OR) (95% CI)		0.9377 (0.5069, 1.7346)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8377
Risk Difference (RD) (95% CI)		-0.0066 (-0.0694, 0.0562)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8376
Grade 3/Severe	1 (0.50)	5 (2.55)
Relative Risk (RR) (95% CI)		5.1531 (0.6075, 43.7115)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1328
Odds Ratio (OR) (95% CI)		5.2618 (0.6092, 45.4502)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1312

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0206 (-0.0035, 0.0447)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0945

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Cough	41 (20.30)	45 (22.96)
Relative Risk (RR) (95% CI)		1.1312 (0.7776, 1.6454)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5192
Odds Ratio (OR) (95% CI)		1.1702 (0.7257, 1.8872)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5191
Risk Difference (RD) (95% CI)		0.0266 (-0.0543, 0.1075)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5189
Grade 1/Mild	33 (16.34)	37 (18.88)
Relative Risk (RR) (95% CI)		1.1555 (0.7546, 1.7696)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5061
Odds Ratio (OR) (95% CI)		1.1917 (0.7108, 1.9982)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5059

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0254 (-0.0494, 0.1002)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5058

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	8 (3.96)	8 (4.08)
Relative Risk (RR) (95% CI)		1.0306 (0.3946, 2.6919)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9509
Odds Ratio (OR) (95% CI)		1.0319 (0.3795, 2.8059)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9509
Risk Difference (RD) (95% CI)		0.0012 (-0.0374, 0.0398)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9509
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Oropharyngeal pain	23 (11.39)	24 (12.24)
Relative Risk (RR) (95% CI)		1.0754 (0.6285, 1.8401)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7907
Odds Ratio (OR) (95% CI)		1.0859 (0.5906, 1.9966)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7907
Risk Difference (RD) (95% CI)		0.0086 (-0.0549, 0.0720)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7908
Grade 1/Mild	19 (9.41)	19 (9.69)
Relative Risk (RR) (95% CI)		1.0306 (0.5629, 1.8869)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9222
Odds Ratio (OR) (95% CI)		1.0339 (0.5298, 2.0177)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9222

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0029 (-0.0549, 0.0606)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9222

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	4 (1.98)	5 (2.55)
Relative Risk (RR) (95% CI)		1.2883 (0.3511, 4.7271)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7025
Odds Ratio (OR) (95% CI)		1.2958 (0.3428, 4.8982)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7025
Risk Difference (RD) (95% CI)		0.0057 (-0.0236, 0.0350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7022
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Nasal congestion	24 (11.88)	19 (9.69)
Relative Risk (RR) (95% CI)		0.8159 (0.4619, 1.4411)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4833
Odds Ratio (OR) (95% CI)		0.7961 (0.4211, 1.5051)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4829
Risk Difference (RD) (95% CI)		-0.0219 (-0.0828, 0.0390)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4813
Grade 1/Mild	20 (9.90)	16 (8.16)
Relative Risk (RR) (95% CI)		0.8245 (0.4403, 1.5439)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5465
Odds Ratio (OR) (95% CI)		0.8089 (0.4062, 1.6110)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5462

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0174 (-0.0736, 0.0389)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5450

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	4 (1.98)	2 (1.02)
Relative Risk (RR) (95% CI)		0.5153 (0.0955, 2.7814)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4409
Odds Ratio (OR) (95% CI)		0.5103 (0.0924, 2.8183)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4404
Risk Difference (RD) (95% CI)		-0.0096 (-0.0334, 0.0142)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4296
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Rhinorrhoea	14 (6.93)	19 (9.69)
Relative Risk (RR) (95% CI)		1.3987 (0.7216, 2.7110)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3204
Odds Ratio (OR) (95% CI)		1.4415 (0.7015, 2.9621)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3197
Risk Difference (RD) (95% CI)		0.0276 (-0.0266, 0.0819)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3181
Grade 1/Mild	13 (6.44)	14 (7.14)
Relative Risk (RR) (95% CI)		1.1099 (0.5355, 2.3005)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7792
Odds Ratio (OR) (95% CI)		1.1183 (0.5117, 2.4442)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7792

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0071 (-0.0424, 0.0565)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7792

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	1 (0.50)	5 (2.55)
Relative Risk (RR) (95% CI)		5.1531 (0.6075, 43.7115)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1328
Odds Ratio (OR) (95% CI)		5.2618 (0.6092, 45.4502)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1312
Risk Difference (RD) (95% CI)		0.0206 (-0.0035, 0.0447)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0945
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Sputum increased	21 (10.40)	18 (9.18)
Relative Risk (RR) (95% CI)		0.8834 (0.4857, 1.6066)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6845
Odds Ratio (OR) (95% CI)		0.8716 (0.4493, 1.6909)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6844
Risk Difference (RD) (95% CI)		-0.0121 (-0.0705, 0.0462)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6839
Grade 1/Mild	16 (7.92)	13 (6.63)
Relative Risk (RR) (95% CI)		0.8374 (0.4138, 1.6946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6217
Odds Ratio (OR) (95% CI)		0.8258 (0.3863, 1.7654)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6215

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0129 (-0.0639, 0.0381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6206

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	5 (2.48)	5 (2.55)
Relative Risk (RR) (95% CI)		1.0306 (0.3031, 3.5046)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9615
Odds Ratio (OR) (95% CI)		1.0314 (0.2939, 3.6197)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9615
Risk Difference (RD) (95% CI)		0.0008 (-0.0300, 0.0315)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9615
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Sinus congestion	5 (2.48)	14 (7.14)
Relative Risk (RR) (95% CI)		2.8857 (1.0594, 7.8601)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0382
Odds Ratio (OR) (95% CI)		3.0308 (1.0704, 8.5817)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0368
Risk Difference (RD) (95% CI)		0.0467 (0.0047, 0.0886)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0292
Grade 1/Mild	4 (1.98)	11 (5.61)
Relative Risk (RR) (95% CI)		2.8342 (0.9179, 8.7506)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0701
Odds Ratio (OR) (95% CI)		2.9432 (0.9210, 9.4056)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0686

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0363 (-0.0012, 0.0738)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0578

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	1 (0.50)	3 (1.53)
Relative Risk (RR) (95% CI)		3.0918 (0.3244, 29.4705)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3265
Odds Ratio (OR) (95% CI)		3.1244 (0.3222, 30.2956)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3257
Risk Difference (RD) (95% CI)		0.0104 (-0.0094, 0.0301)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3035
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Haemoptysis	11 (5.45)	13 (6.63)
Relative Risk (RR) (95% CI)		1.2180 (0.5592, 2.6531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6196
Odds Ratio (OR) (95% CI)		1.2335 (0.5389, 2.8235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6195
Risk Difference (RD) (95% CI)		0.0119 (-0.0350, 0.0587)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6193
Grade 1/Mild	7 (3.47)	7 (3.57)
Relative Risk (RR) (95% CI)		1.0306 (0.3683, 2.8841)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9542
Odds Ratio (OR) (95% CI)		1.0317 (0.3551, 2.9977)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9542

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0011 (-0.0351, 0.0373)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9542

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	4 (1.98)	4 (2.04)
Relative Risk (RR) (95% CI)		1.0306 (0.2614, 4.0635)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9656
Odds Ratio (OR) (95% CI)		1.0313 (0.2543, 4.1821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9656
Risk Difference (RD) (95% CI)		0.0006 (-0.0270, 0.0282)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9656
Grade 3/Severe	0	2 (1.02)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0102 (-0.0039, 0.0243)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1552

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Productive cough	5 (2.48)	12 (6.12)
Relative Risk (RR) (95% CI)		2.4735 (0.8878, 6.8910)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0832
Odds Ratio (OR) (95% CI)		2.5696 (0.8881, 7.4349)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0817
Risk Difference (RD) (95% CI)		0.0365 (-0.0033, 0.0763)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0726
Grade 1/Mild	2 (0.99)	8 (4.08)
Relative Risk (RR) (95% CI)		4.1224 (0.8865, 19.1715)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0709
Odds Ratio (OR) (95% CI)		4.2553 (0.8922, 20.2954)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0692

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0309 (0.0000, 0.0618)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0498

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	3 (1.49)	4 (2.04)
Relative Risk (RR) (95% CI)		1.3741 (0.3116, 6.0607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6746
Odds Ratio (OR) (95% CI)		1.3819 (0.3053, 6.2558)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6746
Risk Difference (RD) (95% CI)		0.0056 (-0.0203, 0.0314)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6740
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Respiration abnormal	5 (2.48)	8 (4.08)
Relative Risk (RR) (95% CI)		1.6490 (0.5489, 4.9535)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3728
Odds Ratio (OR) (95% CI)		1.6766 (0.5389, 5.2166)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3722
Risk Difference (RD) (95% CI)		0.0161 (-0.0190, 0.0511)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3686
Grade 1/Mild	4 (1.98)	5 (2.55)
Relative Risk (RR) (95% CI)		1.2883 (0.3511, 4.7271)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7025
Odds Ratio (OR) (95% CI)		1.2958 (0.3428, 4.8982)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7025

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0057 (-0.0236, 0.0350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7022

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	1 (0.50)	3 (1.53)
Relative Risk (RR) (95% CI)		3.0918 (0.3244, 29.4705)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3265
Odds Ratio (OR) (95% CI)		3.1244 (0.3222, 30.2956)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3257
Risk Difference (RD) (95% CI)		0.0104 (-0.0094, 0.0301)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3035
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [2] Odds ratio from 2x2 table.
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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Dyspnoea	7 (3.47)	7 (3.57)
Relative Risk (RR) (95% CI)		1.0306 (0.3683, 2.8841)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9542
Odds Ratio (OR) (95% CI)		1.0317 (0.3551, 2.9977)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9542
Risk Difference (RD) (95% CI)		0.0011 (-0.0351, 0.0373)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9542
Grade 1/Mild	7 (3.47)	2 (1.02)
Relative Risk (RR) (95% CI)		0.2945 (0.0619, 1.4001)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1243
Odds Ratio (OR) (95% CI)		0.2872 (0.0589, 1.3998)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1226

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0244 (-0.0533, 0.0044)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0971

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	0	5 (2.55)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0255 (0.0034, 0.0476)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0235
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Sputum discoloured	6 (2.97)	4 (2.04)
Relative Risk (RR) (95% CI)		0.6871 (0.1969, 2.3976)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5561
Odds Ratio (OR) (95% CI)		0.6806 (0.1891, 2.4494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5559
Risk Difference (RD) (95% CI)		-0.0093 (-0.0400, 0.0214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5524
Grade 1/Mild	4 (1.98)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0198 (-0.0390, -0.0006)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0434

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	4 (2.04)
Relative Risk (RR) (95% CI)		2.0612 (0.3819, 11.1258)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4004
Odds Ratio (OR) (95% CI)		2.0833 (0.3772, 11.5059)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3999
Risk Difference (RD) (95% CI)		0.0105 (-0.0135, 0.0346)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3918
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Investigations	72 (35.64)	72 (36.73)
Relative Risk (RR) (95% CI)		1.0306 (0.7939, 1.3379)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8208
Odds Ratio (OR) (95% CI)		1.0484 (0.6965, 1.5781)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8208
Risk Difference (RD) (95% CI)		0.0109 (-0.0835, 0.1053)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8208
Grade 1/Mild	41 (20.30)	47 (23.98)
Relative Risk (RR) (95% CI)		1.1814 (0.8162, 1.7102)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3770
Odds Ratio (OR) (95% CI)		1.2387 (0.7708, 1.9906)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3766

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0368 (-0.0447, 0.1184)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3761

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	28 (13.86)	23 (11.73)
Relative Risk (RR) (95% CI)		0.8466 (0.5056, 1.4174)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5265
Odds Ratio (OR) (95% CI)		0.8262 (0.4578, 1.4909)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5261
Risk Difference (RD) (95% CI)		-0.0213 (-0.0868, 0.0443)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5250
Grade 3/Severe	3 (1.49)	2 (1.02)
Relative Risk (RR) (95% CI)		0.6871 (0.1161, 4.0676)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6791
Odds Ratio (OR) (95% CI)		0.6838 (0.1130, 4.1374)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6790

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0046 (-0.0265, 0.0172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6764

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Blood creatine phosphokinase increased	24 (11.88)	18 (9.18)
Relative Risk (RR) (95% CI)		0.7730 (0.4334, 1.3787)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3831
Odds Ratio (OR) (95% CI)		0.7500 (0.3933, 1.4302)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3824
Risk Difference (RD) (95% CI)		-0.0270 (-0.0872, 0.0332)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3799
Grade 1/Mild	18 (8.91)	14 (7.14)
Relative Risk (RR) (95% CI)		0.8016 (0.4101, 1.5668)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5178
Odds Ratio (OR) (95% CI)		0.7863 (0.3797, 1.6282)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5174

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0177 (-0.0710, 0.0356)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5158

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	5 (2.48)	4 (2.04)
Relative Risk (RR) (95% CI)		0.8245 (0.2247, 3.0253)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7711
Odds Ratio (OR) (95% CI)		0.8208 (0.2172, 3.1027)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7710
Risk Difference (RD) (95% CI)		-0.0043 (-0.0335, 0.0248)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7704
Grade 3/Severe	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Alanine aminotransferase increased	11 (5.45)	13 (6.63)
Relative Risk (RR) (95% CI)		1.2180 (0.5592, 2.6531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6196
Odds Ratio (OR) (95% CI)		1.2335 (0.5389, 2.8235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6195
Risk Difference (RD) (95% CI)		0.0119 (-0.0350, 0.0587)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6193
Grade 1/Mild	7 (3.47)	7 (3.57)
Relative Risk (RR) (95% CI)		1.0306 (0.3683, 2.8841)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9542
Odds Ratio (OR) (95% CI)		1.0317 (0.3551, 2.9977)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9542

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0011 (-0.0351, 0.0373)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9542

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	3 (1.49)	6 (3.06)
Relative Risk (RR) (95% CI)		2.0612 (0.5228, 8.1271)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3014
Odds Ratio (OR) (95% CI)		2.0947 (0.5165, 8.4953)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3006
Risk Difference (RD) (95% CI)		0.0158 (-0.0136, 0.0451)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2921
Grade 3/Severe	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [2] Odds ratio from 2x2 table.
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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Aspartate aminotransferase increased	9 (4.46)	12 (6.12)
Relative Risk (RR) (95% CI)		1.3741 (0.5923, 3.1882)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4592
Odds Ratio (OR) (95% CI)		1.3986 (0.5757, 3.3973)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4588
Risk Difference (RD) (95% CI)		0.0167 (-0.0273, 0.0607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4578
Grade 1/Mild	7 (3.47)	6 (3.06)
Relative Risk (RR) (95% CI)		0.8834 (0.3022, 2.5820)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8207
Odds Ratio (OR) (95% CI)		0.8797 (0.2903, 2.6655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8207

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0040 (-0.0389, 0.0309)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8204

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	1 (0.50)	6 (3.06)
Relative Risk (RR) (95% CI)		6.1837 (0.7513, 50.8955)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0903
Odds Ratio (OR) (95% CI)		6.3474 (0.7571, 53.2135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0885
Risk Difference (RD) (95% CI)		0.0257 (-0.0003, 0.0516)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0529
Grade 3/Severe	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Weight decreased	1 (0.50)	9 (4.59)
Relative Risk (RR) (95% CI)		9.2755 (1.1862, 72.5295)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0338
Odds Ratio (OR) (95% CI)		9.6738 (1.2139, 77.0904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0321
Risk Difference (RD) (95% CI)		0.0410 (0.0101, 0.0718)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0093
Grade 1/Mild	1 (0.50)	7 (3.57)
Relative Risk (RR) (95% CI)		7.2143 (0.8958, 58.0972)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0634
Odds Ratio (OR) (95% CI)		7.4444 (0.9074, 61.0777)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0616

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0308 (0.0030, 0.0585)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0296

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	0	2 (1.02)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0102 (-0.0039, 0.0243)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1552
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
SARS-CoV-2 test positive	3 (1.49)	8 (4.08)
Relative Risk (RR) (95% CI)		2.7483 (0.7399, 10.2088)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1311
Odds Ratio (OR) (95% CI)		2.8227 (0.7378, 10.7993)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1296
Risk Difference (RD) (95% CI)		0.0260 (-0.0064, 0.0583)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1155
Grade 1/Mild	1 (0.50)	5 (2.55)
Relative Risk (RR) (95% CI)		5.1531 (0.6075, 43.7115)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1328
Odds Ratio (OR) (95% CI)		5.2618 (0.6092, 45.4502)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1312

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0206 (-0.0035, 0.0447)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0945

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	3 (1.53)
Relative Risk (RR) (95% CI)		1.5459 (0.2611, 9.1521)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6312
Odds Ratio (OR) (95% CI)		1.5544 (0.2569, 9.4045)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6310
Risk Difference (RD) (95% CI)		0.0054 (-0.0165, 0.0274)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6294
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Bacterial test positive	6 (2.97)	7 (3.57)
Relative Risk (RR) (95% CI)		1.2024 (0.4114, 3.5144)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7363
Odds Ratio (OR) (95% CI)		1.2099 (0.3993, 3.6660)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7362
Risk Difference (RD) (95% CI)		0.0060 (-0.0290, 0.0410)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7362
Grade 1/Mild	4 (1.98)	5 (2.55)
Relative Risk (RR) (95% CI)		1.2883 (0.3511, 4.7271)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7025
Odds Ratio (OR) (95% CI)		1.2958 (0.3428, 4.8982)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7025

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0057 (-0.0236, 0.0350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7022

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	2 (1.02)
Relative Risk (RR) (95% CI)		1.0306 (0.1466, 7.2445)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9758
Odds Ratio (OR) (95% CI)		1.0309 (0.1438, 7.3916)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9758
Risk Difference (RD) (95% CI)		0.0003 (-0.0193, 0.0199)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9758
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Blood bilirubin increased	7 (3.47)	4 (2.04)
Relative Risk (RR) (95% CI)		0.5889 (0.1751, 1.9802)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3921
Odds Ratio (OR) (95% CI)		0.5804 (0.1672, 2.0146)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3915
Risk Difference (RD) (95% CI)		-0.0142 (-0.0463, 0.0178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3839
Grade 1/Mild	4 (1.98)	3 (1.53)
Relative Risk (RR) (95% CI)		0.7730 (0.1753, 3.4092)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7338
Odds Ratio (OR) (95% CI)		0.7694 (0.1700, 3.4831)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7337

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0045 (-0.0303, 0.0213)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7325

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	3 (1.49)	1 (0.51)
Relative Risk (RR) (95% CI)		0.3435 (0.0360, 3.2745)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3530
Odds Ratio (OR) (95% CI)		0.3402 (0.0351, 3.2985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3522
Risk Difference (RD) (95% CI)		-0.0097 (-0.0292, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3255
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Gastrointestinal disorders	68 (33.66)	64 (32.65)
Relative Risk (RR) (95% CI)		0.9700 (0.7338, 1.2823)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8306
Odds Ratio (OR) (95% CI)		0.9554 (0.6294, 1.4505)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8305
Risk Difference (RD) (95% CI)		-0.0101 (-0.1026, 0.0824)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8305
Grade 1/Mild	50 (24.75)	45 (22.96)
Relative Risk (RR) (95% CI)		0.9276 (0.6526, 1.3183)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6750
Odds Ratio (OR) (95% CI)		0.9060 (0.5711, 1.4371)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6749

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0179 (-0.1017, 0.0658)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6746

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	18 (8.91)	17 (8.67)
Relative Risk (RR) (95% CI)		0.9734 (0.5168, 1.8332)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9334
Odds Ratio (OR) (95% CI)		0.9708 (0.4850, 1.9434)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9334
Risk Difference (RD) (95% CI)		-0.0024 (-0.0580, 0.0533)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9334
Grade 3/Severe	0	2 (1.02)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0102 (-0.0039, 0.0243)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1552

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Diarrhoea	15 (7.43)	21 (10.71)
Relative Risk (RR) (95% CI)		1.4429 (0.7663, 2.7167)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2561
Odds Ratio (OR) (95% CI)		1.4960 (0.7474, 2.9943)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2552
Risk Difference (RD) (95% CI)		0.0329 (-0.0235, 0.0893)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2532
Grade 1/Mild	15 (7.43)	18 (9.18)
Relative Risk (RR) (95% CI)		1.2367 (0.6415, 2.3843)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5258
Odds Ratio (OR) (95% CI)		1.2607 (0.6165, 2.5778)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5256

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0176 (-0.0367, 0.0718)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5253

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	0	3 (1.53)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0153 (-0.0019, 0.0325)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0809
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Abdominal pain upper	6 (2.97)	12 (6.12)
Relative Risk (RR) (95% CI)		2.0612 (0.7892, 5.3837)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1398
Odds Ratio (OR) (95% CI)		2.1304 (0.7834, 5.7936)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1384
Risk Difference (RD) (95% CI)		0.0315 (-0.0094, 0.0724)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1311
Grade 1/Mild	5 (2.48)	6 (3.06)
Relative Risk (RR) (95% CI)		1.2367 (0.3837, 3.9865)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7220
Odds Ratio (OR) (95% CI)		1.2442 (0.3735, 4.1451)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7219

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0059 (-0.0264, 0.0381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7218

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	1 (0.50)	5 (2.55)
Relative Risk (RR) (95% CI)		5.1531 (0.6075, 43.7115)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1328
Odds Ratio (OR) (95% CI)		5.2618 (0.6092, 45.4502)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1312
Risk Difference (RD) (95% CI)		0.0206 (-0.0035, 0.0447)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0945
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Abdominal pain	14 (6.93)	10 (5.10)
Relative Risk (RR) (95% CI)		0.7362 (0.3350, 1.6177)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4457
Odds Ratio (OR) (95% CI)		0.7220 (0.3128, 1.6664)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4452
Risk Difference (RD) (95% CI)		-0.0183 (-0.0649, 0.0284)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4422
Grade 1/Mild	10 (4.95)	5 (2.55)
Relative Risk (RR) (95% CI)		0.5153 (0.1794, 1.4805)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2182
Odds Ratio (OR) (95% CI)		0.5026 (0.1686, 1.4980)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2170

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0240 (-0.0612, 0.0132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2059

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	4 (1.98)	4 (2.04)
Relative Risk (RR) (95% CI)		1.0306 (0.2614, 4.0635)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9656
Odds Ratio (OR) (95% CI)		1.0313 (0.2543, 4.1821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9656
Risk Difference (RD) (95% CI)		0.0006 (-0.0270, 0.0282)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9656
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Constipation	10 (4.95)	7 (3.57)
Relative Risk (RR) (95% CI)		0.7214 (0.2802, 1.8574)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4986
Odds Ratio (OR) (95% CI)		0.7111 (0.2651, 1.9072)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4982
Risk Difference (RD) (95% CI)		-0.0138 (-0.0534, 0.0258)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4951
Grade 1/Mild	5 (2.48)	6 (3.06)
Relative Risk (RR) (95% CI)		1.2367 (0.3837, 3.9865)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7220
Odds Ratio (OR) (95% CI)		1.2442 (0.3735, 4.1451)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7219

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0059 (-0.0264, 0.0381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7218

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	5 (2.48)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0248 (-0.0462, -0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0236
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Nausea	17 (8.42)	7 (3.57)
Relative Risk (RR) (95% CI)		0.4244 (0.1799, 1.0008)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0502
Odds Ratio (OR) (95% CI)		0.4031 (0.1633, 0.9946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0486
Risk Difference (RD) (95% CI)		-0.0484 (-0.0947, -0.0022)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0402
Grade 1/Mild	14 (6.93)	7 (3.57)
Relative Risk (RR) (95% CI)		0.5153 (0.2125, 1.2495)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1424
Odds Ratio (OR) (95% CI)		0.4974 (0.1963, 1.2599)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1408

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0336 (-0.0772, 0.0100)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1311

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	3 (1.49)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0149 (-0.0315, 0.0018)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0810
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Flatulence	7 (3.47)	6 (3.06)
Relative Risk (RR) (95% CI)		0.8834 (0.3022, 2.5820)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8207
Odds Ratio (OR) (95% CI)		0.8797 (0.2903, 2.6655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8207
Risk Difference (RD) (95% CI)		-0.0040 (-0.0389, 0.0309)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8204
Grade 1/Mild	7 (3.47)	6 (3.06)
Relative Risk (RR) (95% CI)		0.8834 (0.3022, 2.5820)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8207
Odds Ratio (OR) (95% CI)		0.8797 (0.2903, 2.6655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8207

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0040 (-0.0389, 0.0309)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8204

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Abdominal distension	10 (4.95)	5 (2.55)
Relative Risk (RR) (95% CI)		0.5153 (0.1794, 1.4805)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2182
Odds Ratio (OR) (95% CI)		0.5026 (0.1686, 1.4980)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2170
Risk Difference (RD) (95% CI)		-0.0240 (-0.0612, 0.0132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2059
Grade 1/Mild	8 (3.96)	5 (2.55)
Relative Risk (RR) (95% CI)		0.6441 (0.2144, 1.9350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4332
Odds Ratio (OR) (95% CI)		0.6348 (0.2040, 1.9752)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4327

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0141 (-0.0489, 0.0207)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4272

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0099 (-0.0236, 0.0038)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1552
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Vomiting	8 (3.96)	3 (1.53)
Relative Risk (RR) (95% CI)		0.3865 (0.1040, 1.4356)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1556
Odds Ratio (OR) (95% CI)		0.3769 (0.0985, 1.4421)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1541
Risk Difference (RD) (95% CI)		-0.0243 (-0.0562, 0.0076)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1357
Grade 1/Mild	7 (3.47)	2 (1.02)
Relative Risk (RR) (95% CI)		0.2945 (0.0619, 1.4001)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1243
Odds Ratio (OR) (95% CI)		0.2872 (0.0589, 1.3998)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1226

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0244 (-0.0533, 0.0044)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0971

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	1 (0.50)	1 (0.51)
Relative Risk (RR) (95% CI)		1.0306 (0.0649, 16.3624)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9829
Odds Ratio (OR) (95% CI)		1.0308 (0.0640, 16.5951)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9829
Risk Difference (RD) (95% CI)		0.0002 (-0.0137, 0.0140)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9829
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
General disorders and administration site conditions	47 (23.27)	56 (28.57)
Relative Risk (RR) (95% CI)		1.2280 (0.8791, 1.7153)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2285
Odds Ratio (OR) (95% CI)		1.3191 (0.8411, 2.0690)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2277
Risk Difference (RD) (95% CI)		0.0530 (-0.0330, 0.1390)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2267
Grade 1/Mild	37 (18.32)	43 (21.94)
Relative Risk (RR) (95% CI)		1.1977 (0.8084, 1.7746)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3683
Odds Ratio (OR) (95% CI)		1.2533 (0.7667, 2.0488)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3679

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- [2] Odds ratio from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0362 (-0.0425, 0.1150)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3674

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	10 (4.95)	12 (6.12)
Relative Risk (RR) (95% CI)		1.2367 (0.5469, 2.7964)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6098
Odds Ratio (OR) (95% CI)		1.2522 (0.5282, 2.9686)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6096
Risk Difference (RD) (95% CI)		0.0117 (-0.0332, 0.0567)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6094
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Pyrexia	21 (10.40)	24 (12.24)
Relative Risk (RR) (95% CI)		1.1778 (0.6784, 2.0450)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		1.2027 (0.6458, 2.2395)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607
Risk Difference (RD) (95% CI)		0.0185 (-0.0438, 0.0808)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5606
Grade 1/Mild	17 (8.42)	19 (9.69)
Relative Risk (RR) (95% CI)		1.1519 (0.6171, 2.1501)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6571
Odds Ratio (OR) (95% CI)		1.1682 (0.5883, 2.3197)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6570

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0128 (-0.0436, 0.0692)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6570

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	4 (1.98)	5 (2.55)
Relative Risk (RR) (95% CI)		1.2883 (0.3511, 4.7271)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7025
Odds Ratio (OR) (95% CI)		1.2958 (0.3428, 4.8982)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7025
Risk Difference (RD) (95% CI)		0.0057 (-0.0236, 0.0350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7022
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Fatigue	16 (7.92)	18 (9.18)
Relative Risk (RR) (95% CI)		1.1594 (0.6089, 2.2079)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6526
Odds Ratio (OR) (95% CI)		1.1756 (0.5814, 2.3770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6525
Risk Difference (RD) (95% CI)		0.0126 (-0.0423, 0.0676)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6525
Grade 1/Mild	11 (5.45)	12 (6.12)
Relative Risk (RR) (95% CI)		1.1243 (0.5081, 2.4877)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7725
Odds Ratio (OR) (95% CI)		1.1324 (0.4875, 2.6305)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7724

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0068 (-0.0391, 0.0527)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7725

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	5 (2.48)	5 (2.55)
Relative Risk (RR) (95% CI)		1.0306 (0.3031, 3.5046)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9615
Odds Ratio (OR) (95% CI)		1.0314 (0.2939, 3.6197)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9615
Risk Difference (RD) (95% CI)		0.0008 (-0.0300, 0.0315)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9615
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Pain	6 (2.97)	8 (4.08)
Relative Risk (RR) (95% CI)		1.3741 (0.4857, 3.8882)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5492
Odds Ratio (OR) (95% CI)		1.3901 (0.4734, 4.0821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5490
Risk Difference (RD) (95% CI)		0.0111 (-0.0252, 0.0474)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5481
Grade 1/Mild	4 (1.98)	3 (1.53)
Relative Risk (RR) (95% CI)		0.7730 (0.1753, 3.4092)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7338
Odds Ratio (OR) (95% CI)		0.7694 (0.1700, 3.4831)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7337

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0045 (-0.0303, 0.0213)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7325

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	5 (2.55)
Relative Risk (RR) (95% CI)		2.5765 (0.5058, 13.1241)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2545
Odds Ratio (OR) (95% CI)		2.6178 (0.5019, 13.6550)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2535
Risk Difference (RD) (95% CI)		0.0156 (-0.0103, 0.0416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2385
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Musculoskeletal and connective tissue disorders	48 (23.76)	41 (20.92)
Relative Risk (RR) (95% CI)		0.8803 (0.6095, 1.2714)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4967
Odds Ratio (OR) (95% CI)		0.8487 (0.5290, 1.3615)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4962
Risk Difference (RD) (95% CI)		-0.0284 (-0.1102, 0.0533)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4955
Grade 1/Mild	27 (13.37)	29 (14.80)
Relative Risk (RR) (95% CI)		1.1070 (0.6809, 1.7996)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6819
Odds Ratio (OR) (95% CI)		1.1255 (0.6394, 1.9811)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6819

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0143 (-0.0541, 0.0827)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6819

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	21 (10.40)	11 (5.61)
Relative Risk (RR) (95% CI)		0.5398 (0.2674, 1.0899)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0854
Odds Ratio (OR) (95% CI)		0.5125 (0.2402, 1.0933)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0838
Risk Difference (RD) (95% CI)		-0.0478 (-0.1008, 0.0052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0769
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Arthralgia	11 (5.45)	10 (5.10)
Relative Risk (RR) (95% CI)		0.9369 (0.4071, 2.1562)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8782
Odds Ratio (OR) (95% CI)		0.9335 (0.3873, 2.2503)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8782
Risk Difference (RD) (95% CI)		-0.0034 (-0.0473, 0.0405)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8781
Grade 1/Mild	5 (2.48)	6 (3.06)
Relative Risk (RR) (95% CI)		1.2367 (0.3837, 3.9865)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7220
Odds Ratio (OR) (95% CI)		1.2442 (0.3735, 4.1451)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7219

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0059 (-0.0264, 0.0381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7218

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	6 (2.97)	4 (2.04)
Relative Risk (RR) (95% CI)		0.6871 (0.1969, 2.3976)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5561
Odds Ratio (OR) (95% CI)		0.6806 (0.1891, 2.4494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5559
Risk Difference (RD) (95% CI)		-0.0093 (-0.0400, 0.0214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5524
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Back pain	16 (7.92)	9 (4.59)
Relative Risk (RR) (95% CI)		0.5797 (0.2624, 1.2807)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1776
Odds Ratio (OR) (95% CI)		0.5595 (0.2412, 1.2979)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1762
Risk Difference (RD) (95% CI)		-0.0333 (-0.0807, 0.0141)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1686
Grade 1/Mild	9 (4.46)	8 (4.08)
Relative Risk (RR) (95% CI)		0.9161 (0.3608, 2.3262)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8538
Odds Ratio (OR) (95% CI)		0.9125 (0.3448, 2.4152)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8538

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0037 (-0.0434, 0.0360)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8536

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	7 (3.47)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0347 (-0.0599, -0.0094)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0071
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Myalgia	3 (1.49)	7 (3.57)
Relative Risk (RR) (95% CI)		2.4048 (0.6308, 9.1669)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1987
Odds Ratio (OR) (95% CI)		2.4568 (0.6261, 9.6401)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1975
Risk Difference (RD) (95% CI)		0.0209 (-0.0100, 0.0517)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1854
Grade 1/Mild	2 (0.99)	5 (2.55)
Relative Risk (RR) (95% CI)		2.5765 (0.5058, 13.1241)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2545
Odds Ratio (OR) (95% CI)		2.6178 (0.5019, 13.6550)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2535

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0156 (-0.0103, 0.0416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2385

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	1 (0.50)	2 (1.02)
Relative Risk (RR) (95% CI)		2.0612 (0.1884, 22.5492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5535
Odds Ratio (OR) (95% CI)		2.0722 (0.1864, 23.0379)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5533
Risk Difference (RD) (95% CI)		0.0053 (-0.0118, 0.0223)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5465
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Nervous system disorders	34 (16.83)	39 (19.90)
Relative Risk (RR) (95% CI)		1.1822 (0.7800, 1.7916)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4302
Odds Ratio (OR) (95% CI)		1.2274 (0.7380, 2.0414)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4298
Risk Difference (RD) (95% CI)		0.0307 (-0.0454, 0.1067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4295
Grade 1/Mild	25 (12.38)	27 (13.78)
Relative Risk (RR) (95% CI)		1.1131 (0.6702, 1.8485)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6790
Odds Ratio (OR) (95% CI)		1.1311 (0.6312, 2.0271)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6789

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- [2] Odds ratio from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0140 (-0.0523, 0.0803)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6789

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	8 (3.96)	9 (4.59)
Relative Risk (RR) (95% CI)		1.1594 (0.4566, 2.9441)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7557
Odds Ratio (OR) (95% CI)		1.1671 (0.4410, 3.0890)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7557
Risk Difference (RD) (95% CI)		0.0063 (-0.0335, 0.0461)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7557
Grade 3/Severe	1 (0.50)	3 (1.53)
Relative Risk (RR) (95% CI)		3.0918 (0.3244, 29.4705)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3265
Odds Ratio (OR) (95% CI)		3.1244 (0.3222, 30.2956)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3257

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0104 (-0.0094, 0.0301)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3035

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Headache	22 (10.89)	25 (12.76)
Relative Risk (RR) (95% CI)		1.1712 (0.6837, 2.0061)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5651
Odds Ratio (OR) (95% CI)		1.1962 (0.6500, 2.2014)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5649
Risk Difference (RD) (95% CI)		0.0186 (-0.0448, 0.0821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5648
Grade 1/Mild	18 (8.91)	18 (9.18)
Relative Risk (RR) (95% CI)		1.0306 (0.5527, 1.9217)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9244
Odds Ratio (OR) (95% CI)		1.0337 (0.5211, 2.0507)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9244

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0027 (-0.0536, 0.0591)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9244

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- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	3 (1.49)	5 (2.55)
Relative Risk (RR) (95% CI)		1.7177 (0.4161, 7.0907)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4546
Odds Ratio (OR) (95% CI)		1.7365 (0.4093, 7.3663)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4542
Risk Difference (RD) (95% CI)		0.0107 (-0.0170, 0.0383)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4502
Grade 3/Severe	1 (0.50)	2 (1.02)
Relative Risk (RR) (95% CI)		2.0612 (0.1884, 22.5492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5535
Odds Ratio (OR) (95% CI)		2.0722 (0.1864, 23.0379)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5533

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0053 (-0.0118, 0.0223)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5465

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Injury, poisoning and procedural complications	36 (17.82)	36 (18.37)
Relative Risk (RR) (95% CI)		1.0306 (0.6785, 1.5656)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8876
Odds Ratio (OR) (95% CI)		1.0375 (0.6227, 1.7285)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8876
Risk Difference (RD) (95% CI)		0.0055 (-0.0702, 0.0811)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8876
Grade 1/Mild	22 (10.89)	20 (10.20)
Relative Risk (RR) (95% CI)		0.9369 (0.5284, 1.6613)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8236
Odds Ratio (OR) (95% CI)		0.9298 (0.4902, 1.7636)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8235

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0069 (-0.0672, 0.0535)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8234

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	12 (5.94)	16 (8.16)
Relative Risk (RR) (95% CI)		1.3741 (0.6674, 2.8294)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3884
Odds Ratio (OR) (95% CI)		1.4074 (0.6479, 3.0572)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3879
Risk Difference (RD) (95% CI)		0.0222 (-0.0281, 0.0725)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3866
Grade 3/Severe	2 (0.99)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0099 (-0.0236, 0.0038)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1552

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Skin and subcutaneous tissue disorders	35 (17.33)	30 (15.31)
Relative Risk (RR) (95% CI)		0.8834 (0.5654, 1.3803)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5861
Odds Ratio (OR) (95% CI)		0.8623 (0.5061, 1.4692)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5858
Risk Difference (RD) (95% CI)		-0.0202 (-0.0928, 0.0524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5852
Grade 1/Mild	30 (14.85)	23 (11.73)
Relative Risk (RR) (95% CI)		0.7901 (0.4762, 1.3111)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3620
Odds Ratio (OR) (95% CI)		0.7622 (0.4256, 1.3651)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3612

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0312 (-0.0978, 0.0354)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3590

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	5 (2.48)	7 (3.57)
Relative Risk (RR) (95% CI)		1.4429 (0.4658, 4.4697)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5251
Odds Ratio (OR) (95% CI)		1.4593 (0.4552, 4.6776)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5248
Risk Difference (RD) (95% CI)		0.0110 (-0.0227, 0.0446)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5235
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Rash	9 (4.46)	12 (6.12)
Relative Risk (RR) (95% CI)		1.3741 (0.5923, 3.1882)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4592
Odds Ratio (OR) (95% CI)		1.3986 (0.5757, 3.3973)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4588
Risk Difference (RD) (95% CI)		0.0167 (-0.0273, 0.0607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4578
Grade 1/Mild	8 (3.96)	10 (5.10)
Relative Risk (RR) (95% CI)		1.2883 (0.5192, 3.1963)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5848
Odds Ratio (OR) (95% CI)		1.3038 (0.5036, 3.3752)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5847

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0114 (-0.0295, 0.0523)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5843

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	1 (0.50)	2 (1.02)
Relative Risk (RR) (95% CI)		2.0612 (0.1884, 22.5492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5535
Odds Ratio (OR) (95% CI)		2.0722 (0.1864, 23.0379)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5533
Risk Difference (RD) (95% CI)		0.0053 (-0.0118, 0.0223)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5465
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [1] Relative risk from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Acne	8 (3.96)	5 (2.55)
Relative Risk (RR) (95% CI)		0.6441 (0.2144, 1.9350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4332
Odds Ratio (OR) (95% CI)		0.6348 (0.2040, 1.9752)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4327
Risk Difference (RD) (95% CI)		-0.0141 (-0.0489, 0.0207)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4272
Grade 1/Mild	6 (2.97)	4 (2.04)
Relative Risk (RR) (95% CI)		0.6871 (0.1969, 2.3976)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5561
Odds Ratio (OR) (95% CI)		0.6806 (0.1891, 2.4494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5559

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0093 (-0.0400, 0.0214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5524

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	1 (0.51)
Relative Risk (RR) (95% CI)		0.5153 (0.0471, 5.6373)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5870
Odds Ratio (OR) (95% CI)		0.5128 (0.0461, 5.7014)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5868
Risk Difference (RD) (95% CI)		-0.0048 (-0.0217, 0.0121)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5780
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Metabolism and nutrition disorders	18 (8.91)	20 (10.20)
Relative Risk (RR) (95% CI)		1.1451 (0.6249, 2.0985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6610
Odds Ratio (OR) (95% CI)		1.1616 (0.5947, 2.2689)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6610
Risk Difference (RD) (95% CI)		0.0129 (-0.0449, 0.0707)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6609
Grade 1/Mild	12 (5.94)	15 (7.65)
Relative Risk (RR) (95% CI)		1.2883 (0.6188, 2.6819)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4983
Odds Ratio (OR) (95% CI)		1.3122 (0.5980, 2.8794)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4981

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0171 (-0.0324, 0.0666)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4975

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	6 (2.97)	4 (2.04)
Relative Risk (RR) (95% CI)		0.6871 (0.1969, 2.3976)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5561
Odds Ratio (OR) (95% CI)		0.6806 (0.1891, 2.4494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5559
Risk Difference (RD) (95% CI)		-0.0093 (-0.0400, 0.0214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5524
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Hypoglycaemia	7 (3.47)	5 (2.55)
Relative Risk (RR) (95% CI)		0.7362 (0.2376, 2.2804)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5954
Odds Ratio (OR) (95% CI)		0.7292 (0.2275, 2.3376)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5952
Risk Difference (RD) (95% CI)		-0.0091 (-0.0427, 0.0244)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5929
Grade 1/Mild	3 (1.49)	4 (2.04)
Relative Risk (RR) (95% CI)		1.3741 (0.3116, 6.0607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6746
Odds Ratio (OR) (95% CI)		1.3819 (0.3053, 6.2558)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6746

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0056 (-0.0203, 0.0314)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6740

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	4 (1.98)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0198 (-0.0390, -0.0006)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0434
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Psychiatric disorders	34 (16.83)	19 (9.69)
Relative Risk (RR) (95% CI)		0.5759 (0.3404, 0.9744)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0397
Odds Ratio (OR) (95% CI)		0.5304 (0.2912, 0.9663)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0383
Risk Difference (RD) (95% CI)		-0.0714 (-0.1375, -0.0052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0345
Grade 1/Mild	17 (8.42)	10 (5.10)
Relative Risk (RR) (95% CI)		0.6062 (0.2847, 1.2911)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1944
Odds Ratio (OR) (95% CI)		0.5851 (0.2610, 1.3115)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1931

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0331 (-0.0823, 0.0160)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1863

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	14 (6.93)	7 (3.57)
Relative Risk (RR) (95% CI)		0.5153 (0.2125, 1.2495)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1424
Odds Ratio (OR) (95% CI)		0.4974 (0.1963, 1.2599)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1408
Risk Difference (RD) (95% CI)		-0.0336 (-0.0772, 0.0100)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1311
Grade 3/Severe	3 (1.49)	2 (1.02)
Relative Risk (RR) (95% CI)		0.6871 (0.1161, 4.0676)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6791
Odds Ratio (OR) (95% CI)		0.6838 (0.1130, 4.1374)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6790

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0046 (-0.0265, 0.0172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6764

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Depression	7 (3.47)	4 (2.04)
Relative Risk (RR) (95% CI)		0.5889 (0.1751, 1.9802)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3921
Odds Ratio (OR) (95% CI)		0.5804 (0.1672, 2.0146)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3915
Risk Difference (RD) (95% CI)		-0.0142 (-0.0463, 0.0178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3839
Grade 1/Mild	5 (2.48)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0248 (-0.0462, -0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0236

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	4 (2.04)
Relative Risk (RR) (95% CI)		2.0612 (0.3819, 11.1258)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4004
Odds Ratio (OR) (95% CI)		2.0833 (0.3772, 11.5059)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3999
Risk Difference (RD) (95% CI)		0.0105 (-0.0135, 0.0346)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3918
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Insomnia	8 (3.96)	4 (2.04)
Relative Risk (RR) (95% CI)		0.5153 (0.1577, 1.6838)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2724
Odds Ratio (OR) (95% CI)		0.5052 (0.1496, 1.7056)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2714
Risk Difference (RD) (95% CI)		-0.0192 (-0.0526, 0.0142)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2599
Grade 1/Mild	5 (2.48)	4 (2.04)
Relative Risk (RR) (95% CI)		0.8245 (0.2247, 3.0253)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7711
Odds Ratio (OR) (95% CI)		0.8208 (0.2172, 3.1027)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7710

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0043 (-0.0335, 0.0248)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7704

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	3 (1.49)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0149 (-0.0315, 0.0018)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0810
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Immune system disorders	2 (0.99)	8 (4.08)
Relative Risk (RR) (95% CI)		4.1224 (0.8865, 19.1715)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0709
Odds Ratio (OR) (95% CI)		4.2553 (0.8922, 20.2954)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0692
Risk Difference (RD) (95% CI)		0.0309 (0.0000, 0.0618)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0498
Grade 1/Mild	2 (0.99)	3 (1.53)
Relative Risk (RR) (95% CI)		1.5459 (0.2611, 9.1521)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6312
Odds Ratio (OR) (95% CI)		1.5544 (0.2569, 9.4045)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6310

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0054 (-0.0165, 0.0274)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6294

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	0	3 (1.53)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0153 (-0.0019, 0.0325)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0809
Grade 3/Severe	0	2 (1.02)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0102 (-0.0039, 0.0243)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1552

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Eye disorders	9 (4.46)	7 (3.57)
Relative Risk (RR) (95% CI)		0.8016 (0.3045, 2.1103)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6543
Odds Ratio (OR) (95% CI)		0.7942 (0.2899, 2.1761)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6542
Risk Difference (RD) (95% CI)		-0.0088 (-0.0474, 0.0297)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6529
Grade 1/Mild	6 (2.97)	4 (2.04)
Relative Risk (RR) (95% CI)		0.6871 (0.1969, 2.3976)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5561
Odds Ratio (OR) (95% CI)		0.6806 (0.1891, 2.4494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5559

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0093 (-0.0400, 0.0214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5524

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	3 (1.49)	3 (1.53)
Relative Risk (RR) (95% CI)		1.0306 (0.2105, 5.0447)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9703
Odds Ratio (OR) (95% CI)		1.0311 (0.2056, 5.1713)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9703
Risk Difference (RD) (95% CI)		0.0005 (-0.0235, 0.0244)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9703
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Reproductive system and breast disorders	15 (7.43)	7 (3.57)
Relative Risk (RR) (95% CI)		0.4810 (0.2004, 1.1542)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1012
Odds Ratio (OR) (95% CI)		0.4617 (0.1841, 1.1582)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0996
Risk Difference (RD) (95% CI)		-0.0385 (-0.0831, 0.0060)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0897
Grade 1/Mild	12 (5.94)	5 (2.55)
Relative Risk (RR) (95% CI)		0.4294 (0.1541, 1.1964)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1059
Odds Ratio (OR) (95% CI)		0.4145 (0.1433, 1.1993)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1042

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0339 (-0.0733, 0.0055)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0915

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	3 (1.49)	2 (1.02)
Relative Risk (RR) (95% CI)		0.6871 (0.1161, 4.0676)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6791
Odds Ratio (OR) (95% CI)		0.6838 (0.1130, 4.1374)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6790
Risk Difference (RD) (95% CI)		-0.0046 (-0.0265, 0.0172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6764
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Ear and labyrinth disorders	10 (4.95)	5 (2.55)
Relative Risk (RR) (95% CI)		0.5153 (0.1794, 1.4805)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2182
Odds Ratio (OR) (95% CI)		0.5026 (0.1686, 1.4980)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2170
Risk Difference (RD) (95% CI)		-0.0240 (-0.0612, 0.0132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2059
Grade 1/Mild	8 (3.96)	5 (2.55)
Relative Risk (RR) (95% CI)		0.6441 (0.2144, 1.9350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4332
Odds Ratio (OR) (95% CI)		0.6348 (0.2040, 1.9752)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4327

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0141 (-0.0489, 0.0207)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4272

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0099 (-0.0236, 0.0038)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1552
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Renal and urinary disorders	16 (7.92)	5 (2.55)
Relative Risk (RR) (95% CI)		0.3221 (0.1203, 0.8622)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0241
Odds Ratio (OR) (95% CI)		0.3043 (0.1093, 0.8476)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0228
Risk Difference (RD) (95% CI)		-0.0537 (-0.0970, -0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0151
Grade 1/Mild	9 (4.46)	4 (2.04)
Relative Risk (RR) (95% CI)		0.4580 (0.1434, 1.4630)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1876
Odds Ratio (OR) (95% CI)		0.4468 (0.1353, 1.4753)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1862

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0241 (-0.0588, 0.0105)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1721

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	7 (3.47)	1 (0.51)
Relative Risk (RR) (95% CI)		0.1472 (0.0183, 1.1857)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0719
Odds Ratio (OR) (95% CI)		0.1429 (0.0174, 1.1721)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0700
Risk Difference (RD) (95% CI)		-0.0296 (-0.0567, -0.0024)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0327
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with any Grade 3/4/5 TEAEs	14 (6.93)	18 (9.18)
Relative Risk (RR) (95% CI)		1.3251 (0.6779, 2.5901)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4104
Odds Ratio (OR) (95% CI)		1.3579 (0.6558, 2.8119)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4100
Risk Difference (RD) (95% CI)		0.0225 (-0.0310, 0.0760)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4091
Infections and infestations	3 (1.49)	7 (3.57)
Relative Risk (RR) (95% CI)		2.4048 (0.6308, 9.1669)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1987
Odds Ratio (OR) (95% CI)		2.4568 (0.6261, 9.6401)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1975

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0209 (-0.0100, 0.0517)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1854

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.3
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with any serious TEAEs	22 (10.89)	21 (10.71)
Relative Risk (RR) (95% CI)		0.9838 (0.5593, 1.7304)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9547
Odds Ratio (OR) (95% CI)		0.9818 (0.5213, 1.8492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9547
Risk Difference (RD) (95% CI)		-0.0018 (-0.0628, 0.0592)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9547
Infections and infestations	6 (2.97)	9 (4.59)
Relative Risk (RR) (95% CI)		1.5459 (0.5607, 4.2620)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3998
Odds Ratio (OR) (95% CI)		1.5722 (0.5489, 4.5029)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3993

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.3
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0162 (-0.0213, 0.0537)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3968

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with any TEAEs leading to treatment discontinuation	9 (4.46)	4 (2.04)
Relative Risk (RR) (95% CI)		0.4580 (0.1434, 1.4630)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1876
Odds Ratio (OR) (95% CI)		0.4468 (0.1353, 1.4753)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1862
Risk Difference (RD) (95% CI)		-0.0241 (-0.0588, 0.0105)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1721
Investigations	3 (1.49)	2 (1.02)
Relative Risk (RR) (95% CI)		0.6871 (0.1161, 4.0676)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6791
Odds Ratio (OR) (95% CI)		0.6838 (0.1130, 4.1374)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6790

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0046 (-0.0265, 0.0172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6764

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Alanine aminotransferase increased	1 (0.50)	1 (0.51)
Relative Risk (RR) (95% CI)		1.0306 (0.0649, 16.3624)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9829
Odds Ratio (OR) (95% CI)		1.0308 (0.0640, 16.5951)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9829
Risk Difference (RD) (95% CI)		0.0002 (-0.0137, 0.0140)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9829
Aspartate aminotransferase increased	1 (0.50)	1 (0.51)
Relative Risk (RR) (95% CI)		1.0306 (0.0649, 16.3624)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9829
Odds Ratio (OR) (95% CI)		1.0308 (0.0640, 16.5951)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9829
Risk Difference (RD) (95% CI)		0.0002 (-0.0137, 0.0140)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9829

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Blood alkaline phosphatase increased	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Blood creatine phosphokinase increased	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Pulmonary function test decreased	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Immune system disorders	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Hypersensitivity	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Infections and infestations	2 (0.99)	1 (0.51)
Relative Risk (RR) (95% CI)		0.5153 (0.0471, 5.6373)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5870
Odds Ratio (OR) (95% CI)		0.5128 (0.0461, 5.7014)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5868
Risk Difference (RD) (95% CI)		-0.0048 (-0.0217, 0.0121)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5780

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Giardiasis	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Appendicitis	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Meningitis aseptic	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Psychiatric disorders	1 (0.50)	1 (0.51)
Relative Risk (RR) (95% CI)		1.0306 (0.0649, 16.3624)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9829
Odds Ratio (OR) (95% CI)		1.0308 (0.0640, 16.5951)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9829
Risk Difference (RD) (95% CI)		0.0002 (-0.0137, 0.0140)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9829

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- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Anxiety	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Depression	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Suicidal ideation	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Respiratory, thoracic and mediastinal disorders	1 (0.50)	1 (0.51)
Relative Risk (RR) (95% CI)		1.0306 (0.0649, 16.3624)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9829
Odds Ratio (OR) (95% CI)		1.0308 (0.0640, 16.5951)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9829
Risk Difference (RD) (95% CI)		0.0002 (-0.0137, 0.0140)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9829

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Dysphonia	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Sputum increased	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Skin and subcutaneous tissue disorders	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Rash maculo-papular	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Gastrointestinal disorders	3 (1.49)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0149 (-0.0315, 0.0018)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0810
Abdominal pain	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Constipation	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Gastritis	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Pancreatitis	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
General disorders and administration site conditions	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Fatigue	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.5
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events - Total and by Severity
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	13 (6.44)	16 (8.16)
Relative Risk (RR) (95% CI)		1.2684 (0.6268, 2.5670)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5085
Odds Ratio (OR) (95% CI)		1.2923 (0.6045, 2.7627)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5083
Risk Difference (RD) (95% CI)		0.0173 (-0.0339, 0.0684)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5078
Subjects with non-severe events (Maximum Grade 1/2)	11 (5.45)	16 (8.16)
Relative Risk (RR) (95% CI)		1.4991 (0.7137, 3.1485)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2850
Odds Ratio (OR) (95% CI)		1.5434 (0.6975, 3.4151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2841
Risk Difference (RD) (95% CI)		0.0272 (-0.0223, 0.0767)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2817

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.5
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events - Total and by Severity
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with severe events (Maximum Grade 3/4/5)	2 (0.99)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0099 (-0.0236, 0.0038)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1552
Subjects with serious events	2 (0.99)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0099 (-0.0236, 0.0038)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1552

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.6
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events - Total and by Severity
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	24 (11.88)	18 (9.18)
Relative Risk (RR) (95% CI)		0.7730 (0.4334, 1.3787)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3831
Odds Ratio (OR) (95% CI)		0.7500 (0.3933, 1.4302)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3824
Risk Difference (RD) (95% CI)		-0.0270 (-0.0872, 0.0332)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3799
Subjects with non-severe events (Maximum Grade 1/2)	23 (11.39)	18 (9.18)
Relative Risk (RR) (95% CI)		0.8066 (0.4495, 1.4473)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4711
Odds Ratio (OR) (95% CI)		0.7870 (0.4105, 1.5087)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4707
Risk Difference (RD) (95% CI)		-0.0220 (-0.0816, 0.0376)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4690

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.6
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events - Total and by Severity
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with severe events (Maximum Grade 3/4/5)	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Subjects with serious events	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.7
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events - Total and by Severity
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with any Treatment-emergent Rash Events	15 (7.43)	17 (8.67)
Relative Risk (RR) (95% CI)		1.1680 (0.6001, 2.2733)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6476
Odds Ratio (OR) (95% CI)		1.1840 (0.5740, 2.4420)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6475
Risk Difference (RD) (95% CI)		0.0125 (-0.0410, 0.0660)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6475
Subjects with non-severe events (Maximum Grade 1/2)	15 (7.43)	17 (8.67)
Relative Risk (RR) (95% CI)		1.1680 (0.6001, 2.2733)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6476
Odds Ratio (OR) (95% CI)		1.1840 (0.5740, 2.4420)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6475
Risk Difference (RD) (95% CI)		0.0125 (-0.0410, 0.0660)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6475

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.7
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events - Total and by Severity
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.8
Study VX20-121-102: Summary of AESI: Treatment-emergent Cataract Events - Total and by Severity
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.9
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events - Total and by Severity
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	7 (3.47)	5 (2.55)
Relative Risk (RR) (95% CI)		0.7362 (0.2376, 2.2804)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5954
Odds Ratio (OR) (95% CI)		0.7292 (0.2275, 2.3376)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5952
Risk Difference (RD) (95% CI)		-0.0091 (-0.0427, 0.0244)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5929
Subjects with non-severe events (Maximum Grade 1/2)	7 (3.47)	4 (2.04)
Relative Risk (RR) (95% CI)		0.5889 (0.1751, 1.9802)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3921
Odds Ratio (OR) (95% CI)		0.5804 (0.1672, 2.0146)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3915
Risk Difference (RD) (95% CI)		-0.0142 (-0.0463, 0.0178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3839

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.9
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events - Total and by Severity
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with severe events (Maximum Grade 3/4/5)	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.10
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events - Total and by Severity
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	28 (13.86)	17 (8.67)
Relative Risk (RR) (95% CI)		0.6257 (0.3540, 1.1061)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1067
Odds Ratio (OR) (95% CI)		0.5902 (0.3119, 1.1167)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1051
Risk Difference (RD) (95% CI)		-0.0519 (-0.1137, 0.0100)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1001
Subjects with non-severe events (Maximum Grade 1/2)	25 (12.38)	15 (7.65)
Relative Risk (RR) (95% CI)		0.6184 (0.3363, 1.1372)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1220
Odds Ratio (OR) (95% CI)		0.5867 (0.2994, 1.1499)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1204
Risk Difference (RD) (95% CI)		-0.0472 (-0.1059, 0.0115)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1149

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.10
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events - Total and by Severity
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with severe events (Maximum Grade 3/4/5)	3 (1.49)	2 (1.02)
Relative Risk (RR) (95% CI)		0.6871 (0.1161, 4.0676)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6791
Odds Ratio (OR) (95% CI)		0.6838 (0.1130, 4.1374)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6790
Risk Difference (RD) (95% CI)		-0.0046 (-0.0265, 0.0172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6764
Subjects with serious events	2 (0.99)	3 (1.53)
Relative Risk (RR) (95% CI)		1.5459 (0.2611, 9.1521)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6312
Odds Ratio (OR) (95% CI)		1.5544 (0.2569, 9.4045)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6310
Risk Difference (RD) (95% CI)		0.0054 (-0.0165, 0.0274)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6294

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.11
Study VX20-121-102: Summary of Death
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)

No data met the criteria for this table.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.12
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events - Total and by Severity
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	70 (34.65)	57 (29.08)
Relative Risk (RR) (95% CI)		0.8392 (0.6284, 1.1207)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2349
Odds Ratio (OR) (95% CI)		0.7733 (0.5065, 1.1805)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2336
Risk Difference (RD) (95% CI)		-0.0557 (-0.1471, 0.0357)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2320
Subjects with non-severe events (Maximum Grade 1/2)	61 (30.20)	52 (26.53)
Relative Risk (RR) (95% CI)		0.8786 (0.6422, 1.2019)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4181
Odds Ratio (OR) (95% CI)		0.8347 (0.5393, 1.2919)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4175
Risk Difference (RD) (95% CI)		-0.0367 (-0.1252, 0.0518)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4166

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.12
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events - Total and by Severity
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with severe events (Maximum Grade 3/4/5)	9 (4.46)	5 (2.55)
Relative Risk (RR) (95% CI)		0.5726 (0.1953, 1.6783)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3095
Odds Ratio (OR) (95% CI)		0.5614 (0.1848, 1.7057)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3086
Risk Difference (RD) (95% CI)		-0.0190 (-0.0551, 0.0170)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3000
Subjects with serious events	23 (11.39)	11 (5.61)
Relative Risk (RR) (95% CI)		0.4929 (0.2470, 0.9838)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0448
Odds Ratio (OR) (95% CI)		0.4627 (0.2192, 0.9770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0433
Risk Difference (RD) (95% CI)		-0.0577 (-0.1121, -0.0034)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0374

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Subjects with any TEAEs	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.3533
Age at screening (<18 years vs. ≥18 years)	0.5689
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.9338
Sex (Male vs. Female)	0.0768
Region (North America vs. Rest of the World)	0.4257

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 1.3.2.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Respiratory, thoracic and mediastinal disorders	
Sinus congestion	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.0111
Age at screening (<18 years vs. ≥18 years)	0.1050
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	>0.9999
Sex (Male vs. Female)	0.3432
Region (North America vs. Rest of the World)	0.0946

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 1.3.2.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Investigations	
Weight decreased	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	>0.9999
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 1.3.2.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Psychiatric disorders	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.1233
Age at screening (<18 years vs. ≥18 years)	0.0539
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.2156
Sex (Male vs. Female)	0.6266
Region (North America vs. Rest of the World)	0.1936

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 1.3.2.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Renal and urinary disorders	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.5852
Age at screening (<18 years vs. ≥18 years)	0.3138
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	>0.9999
Sex (Male vs. Female)	0.1878
Region (North America vs. Rest of the World)	0.3814

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Subjects with any TEAEs	111 (97.37)	99 (98.02)
Relative Risk (RR) (95% CI)		1.0067 (0.9663, 1.0488)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7498
Odds Ratio (OR) (95% CI)		1.3378 (0.2190, 8.1715)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7526
Risk Difference (RD) (95% CI)		0.0065 (-0.0335, 0.0465)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7497
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	0	7 (6.93)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0693 (0.0198, 0.1188)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0061
Psychiatric disorders	21 (18.42)	7 (6.93)
Relative Risk (RR) (95% CI)		0.3762 (0.1670, 0.8478)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0184
Odds Ratio (OR) (95% CI)		0.3298 (0.1338, 0.8129)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0160
Risk Difference (RD) (95% CI)		-0.1149 (-0.2016, -0.0282)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0094

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Renal and urinary disorders	11 (9.65)	2 (1.98)
Relative Risk (RR) (95% CI)		0.2052 (0.0466, 0.9039)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0363
Odds Ratio (OR) (95% CI)		0.1892 (0.0409, 0.8751)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0331
Risk Difference (RD) (95% CI)		-0.0767 (-0.1373, -0.0161)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0132

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Subjects with any TEAEs	80 (91.95)	81 (88.04)
Relative Risk (RR) (95% CI)		0.9575 (0.8684, 1.0557)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3830
Odds Ratio (OR) (95% CI)		0.6443 (0.2378, 1.7457)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3874
Risk Difference (RD) (95% CI)		-0.0391 (-0.1266, 0.0484)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3812
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	5 (5.75)	7 (7.61)
Relative Risk (RR) (95% CI)		1.3239 (0.4365, 4.0155)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6201

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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Odds Ratio (OR) (95% CI)		1.3506 (0.4121, 4.4265)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6197
Risk Difference (RD) (95% CI)		0.0186 (-0.0544, 0.0916)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6171
Psychiatric disorders	13 (14.94)	12 (13.04)
Relative Risk (RR) (95% CI)		0.8729 (0.4216, 1.8074)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7143
Odds Ratio (OR) (95% CI)		0.8538 (0.3664, 1.9895)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7143
Risk Difference (RD) (95% CI)		-0.0190 (-0.1207, 0.0827)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7144

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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Renal and urinary disorders	5 (5.75)	2 (2.17)
Relative Risk (RR) (95% CI)		0.3783 (0.0754, 1.8988)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2376
Odds Ratio (OR) (95% CI)		0.3644 (0.0688, 1.9300)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2353
Risk Difference (RD) (95% CI)		-0.0357 (-0.0930, 0.0215)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2214

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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with any TEAEs	28 (90.32)	22 (84.62)
Relative Risk (RR) (95% CI)		0.9368 (0.7667, 1.1446)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5231
Odds Ratio (OR) (95% CI)		0.5893 (0.1192, 2.9121)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5165
Risk Difference (RD) (95% CI)		-0.0571 (-0.2305, 0.1163)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5189
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	1 (3.23)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0323 (-0.0945, 0.0299)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3094
Investigations		
Weight decreased	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- A subject with multiple events within a category is counted only once in that category.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Psychiatric disorders	2 (6.45)	4 (15.38)
Relative Risk (RR) (95% CI)		2.3846 (0.4741, 11.9940)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2917
Odds Ratio (OR) (95% CI)		2.6364 (0.4421, 15.7202)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2873
Risk Difference (RD) (95% CI)		0.0893 (-0.0741, 0.2528)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2841
Renal and urinary disorders	2 (6.45)	0

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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0645 (-0.1510, 0.0220)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1437

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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any TEAEs	163 (95.32)	161 (94.71)
Relative Risk (RR) (95% CI)		0.9935 (0.9464, 1.0431)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7940
Odds Ratio (OR) (95% CI)		0.8780 (0.3305, 2.3322)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7940
Risk Difference (RD) (95% CI)		-0.0062 (-0.0524, 0.0400)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7939
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	4 (2.34)	14 (8.24)
Relative Risk (RR) (95% CI)		3.5206 (1.1828, 10.4788)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0237

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Odds Ratio (OR) (95% CI)		3.7468 (1.2074, 11.6269)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0222
Risk Difference (RD) (95% CI)		0.0590 (0.0118, 0.1061)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0142
Investigations		
Weight decreased	1 (0.58)	9 (5.29)
Relative Risk (RR) (95% CI)		9.0529 (1.1596, 70.6783)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0356
Odds Ratio (OR) (95% CI)		9.5031 (1.1906, 75.8543)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0336

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Risk Difference (RD) (95% CI)		0.0471 (0.0115, 0.0826)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0094
Psychiatric disorders	32 (18.71)	15 (8.82)
Relative Risk (RR) (95% CI)		0.4715 (0.2652, 0.8383)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0104
Odds Ratio (OR) (95% CI)		0.4204 (0.2184, 0.8090)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0095
Risk Difference (RD) (95% CI)		-0.0989 (-0.1713, -0.0265)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0074
Renal and urinary disorders	14 (8.19)	5 (2.94)

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Relative Risk (RR) (95% CI)		0.3592 (0.1323, 0.9754)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0445
Odds Ratio (OR) (95% CI)		0.3398 (0.1196, 0.9655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0428
Risk Difference (RD) (95% CI)		-0.0525 (-0.1008, -0.0042)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0333

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with any TEAEs	18 (94.74)	16 (94.12)
Relative Risk (RR) (95% CI)		0.9935 (0.8472, 1.1649)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9357
Odds Ratio (OR) (95% CI)		0.8889 (0.0513, 15.4045)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9355
Risk Difference (RD) (95% CI)		-0.0062 (-0.1565, 0.1441)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9356
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Psychiatric disorders	1 (5.26)	2 (11.76)
Relative Risk (RR) (95% CI)		2.2353 (0.2220, 22.5093)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4948
Odds Ratio (OR) (95% CI)		2.4000 (0.1977, 29.1311)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4919
Risk Difference (RD) (95% CI)		0.0650 (-0.1181, 0.2481)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4865

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Renal and urinary disorders	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with any TEAEs	172 (94.51)	165 (93.22)
Relative Risk (RR) (95% CI)		0.9864 (0.9355, 1.0401)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6124
Odds Ratio (OR) (95% CI)		0.7994 (0.3363, 1.9004)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6124
Risk Difference (RD) (95% CI)		-0.0129 (-0.0625, 0.0368)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6121
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	5 (2.75)	13 (7.34)
Relative Risk (RR) (95% CI)		2.6734 (0.9733, 7.3434)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0565

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Odds Ratio (OR) (95% CI)		2.8061 (0.9790, 8.0433)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0548
Risk Difference (RD) (95% CI)		0.0460 (0.0008, 0.0911)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0461
Psychiatric disorders	33 (18.13)	17 (9.60)
Relative Risk (RR) (95% CI)		0.5297 (0.3064, 0.9157)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0229
Odds Ratio (OR) (95% CI)		0.4797 (0.2565, 0.8974)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0215
Risk Difference (RD) (95% CI)		-0.0853 (-0.1561, -0.0144)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0183

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Renal and urinary disorders	16 (8.79)	5 (2.82)
Relative Risk (RR) (95% CI)		0.3213 (0.1203, 0.8584)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0235
Odds Ratio (OR) (95% CI)		0.3016 (0.1080, 0.8419)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0221
Risk Difference (RD) (95% CI)		-0.0597 (-0.1075, -0.0118)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0145

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Male

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Subjects with any TEAEs	112 (94.12)	112 (96.55)
Relative Risk (RR) (95% CI)		1.0259 (0.9694, 1.0856)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3764
Odds Ratio (OR) (95% CI)		1.7500 (0.4983, 6.1454)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3825
Risk Difference (RD) (95% CI)		0.0243 (-0.0294, 0.0781)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3748
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	2 (1.68)	9 (7.76)
Relative Risk (RR) (95% CI)		4.6164 (1.0191, 20.9114)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0472

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Male

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Odds Ratio (OR) (95% CI)		4.9206 (1.0397, 23.2863)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0445
Risk Difference (RD) (95% CI)		0.0608 (0.0069, 0.1147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0270
Psychiatric disorders	20 (16.81)	10 (8.62)
Relative Risk (RR) (95% CI)		0.5129 (0.2510, 1.0482)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0671
Odds Ratio (OR) (95% CI)		0.4670 (0.2084, 1.0466)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0644
Risk Difference (RD) (95% CI)		-0.0819 (-0.1663, 0.0025)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0573

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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Male

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Renal and urinary disorders	14 (11.76)	3 (2.59)
Relative Risk (RR) (95% CI)		0.2198 (0.0649, 0.7449)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0150
Odds Ratio (OR) (95% CI)		0.1991 (0.0556, 0.7125)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0131
Risk Difference (RD) (95% CI)		-0.0918 (-0.1565, -0.0271)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0054

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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Female

System Organ Class Preferred Term	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Subjects with any TEAEs	79 (95.18)	71 (88.75)
Relative Risk (RR) (95% CI)		0.9324 (0.8506, 1.0221)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1354
Odds Ratio (OR) (95% CI)		0.3994 (0.1179, 1.3538)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1406
Risk Difference (RD) (95% CI)		-0.0643 (-0.1475, 0.0189)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1297
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	3 (3.61)	5 (6.25)
Relative Risk (RR) (95% CI)		1.7292 (0.4272, 6.9983)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4426

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Female

System Organ Class Preferred Term	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Odds Ratio (OR) (95% CI)		1.7778 (0.4106, 7.6981)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4416
Risk Difference (RD) (95% CI)		0.0264 (-0.0402, 0.0929)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4375
Psychiatric disorders	14 (16.87)	9 (11.25)
Relative Risk (RR) (95% CI)		0.6670 (0.3060, 1.4536)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3082
Odds Ratio (OR) (95% CI)		0.6247 (0.2539, 1.5375)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3059
Risk Difference (RD) (95% CI)		-0.0562 (-0.1624, 0.0501)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3000

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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Female

System Organ Class Preferred Term	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Renal and urinary disorders	2 (2.41)	2 (2.50)
Relative Risk (RR) (95% CI)		1.0375 (0.1497, 7.1891)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9703
Odds Ratio (OR) (95% CI)		1.0385 (0.1427, 7.5550)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9703
Risk Difference (RD) (95% CI)		0.0009 (-0.0466, 0.0484)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9703

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = North America

System Organ Class Preferred Term	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Subjects with any TEAEs	86 (94.51)	83 (95.40)
Relative Risk (RR) (95% CI)		1.0095 (0.9434, 1.0802)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7845
Odds Ratio (OR) (95% CI)		1.2064 (0.3131, 4.6486)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7851
Risk Difference (RD) (95% CI)		0.0090 (-0.0553, 0.0732)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7844
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	5 (5.49)	10 (11.49)
Relative Risk (RR) (95% CI)		2.0920 (0.7450, 5.8744)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1612

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = North America

System Organ Class Preferred Term	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Odds Ratio (OR) (95% CI)		2.2338 (0.7312, 6.8235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1584
Risk Difference (RD) (95% CI)		0.0600 (-0.0218, 0.1418)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1503
Psychiatric disorders	14 (15.38)	11 (12.64)
Relative Risk (RR) (95% CI)		0.8218 (0.3949, 1.7105)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5998
Odds Ratio (OR) (95% CI)		0.7961 (0.3399, 1.8642)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5993
Risk Difference (RD) (95% CI)		-0.0274 (-0.1293, 0.0744)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5979

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = North America

System Organ Class Preferred Term	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Renal and urinary disorders	10 (10.99)	2 (2.30)
Relative Risk (RR) (95% CI)		0.2092 (0.0472, 0.9277)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0395
Odds Ratio (OR) (95% CI)		0.1906 (0.0405, 0.8965)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0359
Risk Difference (RD) (95% CI)		-0.0869 (-0.1585, -0.0153)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0173

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

System Organ Class Preferred Term	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Subjects with any TEAEs	105 (94.59)	100 (91.74)
Relative Risk (RR) (95% CI)		0.9699 (0.9027, 1.0420)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4032
Odds Ratio (OR) (95% CI)		0.6349 (0.2181, 1.8486)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4048
Risk Difference (RD) (95% CI)		-0.0285 (-0.0951, 0.0381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4016
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	0	4 (3.67)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

System Organ Class Preferred Term	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0367 (0.0014, 0.0720)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0416
Psychiatric disorders	20 (18.02)	8 (7.34)
Relative Risk (RR) (95% CI)		0.4073 (0.1874, 0.8852)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0233
Odds Ratio (OR) (95% CI)		0.3604 (0.1514, 0.8581)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0211
Risk Difference (RD) (95% CI)		-0.1068 (-0.1934, -0.0201)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0157

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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

System Organ Class Preferred Term	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Renal and urinary disorders	6 (5.41)	3 (2.75)
Relative Risk (RR) (95% CI)		0.5092 (0.1306, 1.9848)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3309
Odds Ratio (OR) (95% CI)		0.4953 (0.1207, 2.0326)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3294
Risk Difference (RD) (95% CI)		-0.0265 (-0.0786, 0.0256)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3181

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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
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Table 1.3.2.2.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Grade 3/4/5 TEAEs by SOC and PT
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Subjects with any Grade 3/4/5 TEAEs	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.5128
Age at screening (<18 years vs. ≥18 years)	0.4712
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.0136
Sex (Male vs. Female)	0.7569
Region (North America vs. Rest of the World)	0.4202

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by "*".
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Subjects with any Grade 3/4/5 TEAEs	11 (9.65)	11 (10.89)
Relative Risk (RR) (95% CI)		1.1287 (0.5114, 2.4911)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7644
Odds Ratio (OR) (95% CI)		1.1444 (0.4736, 2.7655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7644
Risk Difference (RD) (95% CI)		0.0124 (-0.0690, 0.0938)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7650

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- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Subjects with any Grade 3/4/5 TEAEs	3 (3.45)	6 (6.52)
Relative Risk (RR) (95% CI)		1.8913 (0.4881, 7.3289)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3565
Odds Ratio (OR) (95% CI)		1.9535 (0.4731, 8.0668)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3547
Risk Difference (RD) (95% CI)		0.0307 (-0.0326, 0.0941)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3418

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Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with any Grade 3/4/5 TEAEs	2 (6.45)	1 (3.85)
Relative Risk (RR) (95% CI)		0.5962 (0.0572, 6.2086)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6653
Odds Ratio (OR) (95% CI)		0.5800 (0.0496, 6.7843)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6642
Risk Difference (RD) (95% CI)		-0.0261 (-0.1398, 0.0877)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6535

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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any Grade 3/4/5 TEAEs	12 (7.02)	17 (10.00)
Relative Risk (RR) (95% CI)		1.4250 (0.7021, 2.8922)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3267
Odds Ratio (OR) (95% CI)		1.4722 (0.6806, 3.1847)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3259
Risk Difference (RD) (95% CI)		0.0298 (-0.0293, 0.0890)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3231

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with any Grade 3/4/5 TEAEs	0	4 (23.53)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.2353 (0.0337, 0.4369)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0222

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with any Grade 3/4/5 TEAEs	14 (7.69)	13 (7.34)
Relative Risk (RR) (95% CI)		0.9548 (0.4620, 1.9734)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9006
Odds Ratio (OR) (95% CI)		0.9512 (0.4339, 2.0854)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9006
Risk Difference (RD) (95% CI)		-0.0035 (-0.0580, 0.0511)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9006

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- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Male

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Subjects with any Grade 3/4/5 TEAEs	7 (5.88)	10 (8.62)
Relative Risk (RR) (95% CI)		1.4655 (0.5774, 3.7196)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4212
Odds Ratio (OR) (95% CI)		1.5094 (0.5543, 4.1102)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4205
Risk Difference (RD) (95% CI)		0.0274 (-0.0389, 0.0937)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4182

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Female

System Organ Class Preferred Term	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Subjects with any Grade 3/4/5 TEAEs	7 (8.43)	8 (10.00)
Relative Risk (RR) (95% CI)		1.1857 (0.4509, 3.1178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7298
Odds Ratio (OR) (95% CI)		1.2063 (0.4161, 3.4972)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7298
Risk Difference (RD) (95% CI)		0.0157 (-0.0732, 0.1045)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7297

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = North America

System Organ Class Preferred Term	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Subjects with any Grade 3/4/5 TEAEs	9 (9.89)	9 (10.34)
Relative Risk (RR) (95% CI)		1.0460 (0.4356, 2.5116)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9199
Odds Ratio (OR) (95% CI)		1.0513 (0.3967, 2.7859)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9199
Risk Difference (RD) (95% CI)		0.0045 (-0.0841, 0.0932)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9199

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

System Organ Class Preferred Term	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Subjects with any Grade 3/4/5 TEAEs	5 (4.50)	9 (8.26)
Relative Risk (RR) (95% CI)		1.8330 (0.6346, 5.2950)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2629
Odds Ratio (OR) (95% CI)		1.9080 (0.6183, 5.8879)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2611
Risk Difference (RD) (95% CI)		0.0375 (-0.0270, 0.1020)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2541

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Serious TEAEs by SOC and PT
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Subjects with any TEAEs	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.4570
Age at screening (<18 years vs. ≥18 years)	0.3688
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.0264
Sex (Male vs. Female)	0.8530
Region (North America vs. Rest of the World)	0.8550

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by "*".
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Subjects with any serious TEAEs	14 (12.28)	14 (13.86)
Relative Risk (RR) (95% CI)		1.1287 (0.5657, 2.2519)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7312
Odds Ratio (OR) (95% CI)		1.1494 (0.5193, 2.5443)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7312
Risk Difference (RD) (95% CI)		0.0158 (-0.0746, 0.1062)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7318

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Subjects with any serious TEAEs	8 (9.20)	6 (6.52)
Relative Risk (RR) (95% CI)		0.7092 (0.2565, 1.9612)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5079
Odds Ratio (OR) (95% CI)		0.6890 (0.2289, 2.0732)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5074
Risk Difference (RD) (95% CI)		-0.0267 (-0.1057, 0.0522)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5068

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with any serious TEAEs	3 (9.68)	1 (3.85)
Relative Risk (RR) (95% CI)		0.3974 (0.0439, 3.5952)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4115
Odds Ratio (OR) (95% CI)		0.3733 (0.0364, 3.8239)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4065
Risk Difference (RD) (95% CI)		-0.0583 (-0.1860, 0.0693)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3706

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any serious TEAEs	19 (11.11)	20 (11.76)
Relative Risk (RR) (95% CI)		1.0588 (0.5864, 1.9119)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8496
Odds Ratio (OR) (95% CI)		1.0667 (0.5474, 2.0787)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8496
Risk Difference (RD) (95% CI)		0.0065 (-0.0610, 0.0741)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8496

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with any serious TEAEs	1 (5.26)	5 (29.41)
Relative Risk (RR) (95% CI)		5.5882 (0.7231, 43.1879)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0991
Odds Ratio (OR) (95% CI)		7.5000 (0.7765, 72.4419)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0816
Risk Difference (RD) (95% CI)		0.2415 (0.0028, 0.4802)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0474

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with any serious TEAEs	21 (11.54)	15 (8.47)
Relative Risk (RR) (95% CI)		0.7345 (0.3914, 1.3783)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3366
Odds Ratio (OR) (95% CI)		0.7099 (0.3534, 1.4260)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3357
Risk Difference (RD) (95% CI)		-0.0306 (-0.0926, 0.0313)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3324

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- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Male

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Subjects with any serious TEAEs	11 (9.24)	10 (8.62)
Relative Risk (RR) (95% CI)		0.9326 (0.4119, 2.1118)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8671
Odds Ratio (OR) (95% CI)		0.9262 (0.3776, 2.2721)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8671
Risk Difference (RD) (95% CI)		-0.0062 (-0.0791, 0.0667)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8670

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Female

System Organ Class Preferred Term	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Subjects with any serious TEAEs	11 (13.25)	11 (13.75)
Relative Risk (RR) (95% CI)		1.0375 (0.4769, 2.2571)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9260
Odds Ratio (OR) (95% CI)		1.0435 (0.4248, 2.5629)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9260
Risk Difference (RD) (95% CI)		0.0050 (-0.1000, 0.1099)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9261

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = North America

System Organ Class Preferred Term	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Subjects with any serious TEAEs	9 (9.89)	9 (10.34)
Relative Risk (RR) (95% CI)		1.0460 (0.4356, 2.5116)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9199
Odds Ratio (OR) (95% CI)		1.0513 (0.3967, 2.7859)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9199
Risk Difference (RD) (95% CI)		0.0045 (-0.0841, 0.0932)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9199

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

System Organ Class Preferred Term	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Subjects with any serious TEAEs	13 (11.71)	12 (11.01)
Relative Risk (RR) (95% CI)		0.9400 (0.4490, 1.9678)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8696
Odds Ratio (OR) (95% CI)		0.9326 (0.4053, 2.1458)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8696
Risk Difference (RD) (95% CI)		-0.0070 (-0.0909, 0.0768)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8696

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for TEAEs Leading to Treatment Discontinuation
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any TEAEs leading to treatment discontinuation	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	0.2278
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	N/C
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with any TEAEs leading to treatment discontinuation	2 (6.45)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0645 (-0.1510, 0.0220)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1437

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any TEAEs leading to treatment discontinuation	7 (4.09)	4 (2.35)
Relative Risk (RR) (95% CI)		0.5748 (0.1714, 1.9275)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3697
Odds Ratio (OR) (95% CI)		0.5645 (0.1622, 1.9651)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3690
Risk Difference (RD) (95% CI)		-0.0174 (-0.0548, 0.0200)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3621

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with any TEAEs leading to treatment discontinuation	0	2 (11.76)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.1176 (-0.0355, 0.2708)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1322

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with any TEAEs leading to treatment discontinuation	9 (4.95)	2 (1.13)
Relative Risk (RR) (95% CI)		0.2285 (0.0501, 1.0428)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0567
Odds Ratio (OR) (95% CI)		0.2197 (0.0468, 1.0314)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0548
Risk Difference (RD) (95% CI)		-0.0382 (-0.0733, -0.0030)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0333

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Elevated Transaminase Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any Treatment-emergent Elevated Transaminase Events	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.7515
Age at screening (<18 years vs. ≥18 years)	0.5562
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.0963
Sex (Male vs. Female)	0.9655
Region (North America vs. Rest of the World)	0.8596

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.5.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Elevated Transaminase Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with non-severe events (Maximum Grade 1/2)	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.7355
Age at screening (<18 years vs. ≥18 years)	0.7221
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.1186
Sex (Male vs. Female)	0.7863
Region (North America vs. Rest of the World)	0.7827

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.5.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Elevated Transaminase Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with severe events (Maximum Grade 3/4/5)	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.5.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Elevated Transaminase Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with serious events	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	7 (6.14)	7 (6.93)
Relative Risk (RR) (95% CI)		1.1287 (0.4099, 3.1078)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8148
Odds Ratio (OR) (95% CI)		1.1383 (0.3851, 3.3642)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8148
Risk Difference (RD) (95% CI)		0.0079 (-0.0584, 0.0742)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8153
Subjects with non-severe events (Maximum Grade 1/2)	6 (5.26)	7 (6.93)
Relative Risk (RR) (95% CI)		1.3168 (0.4576, 3.7896)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6098
Odds Ratio (OR) (95% CI)		1.3404 (0.4352, 4.1285)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6097

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- A subject with multiple events within a category is counted only once in that category.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Risk Difference (RD) (95% CI)		0.0167 (-0.0476, 0.0810)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6112
Subjects with severe events (Maximum Grade 3/4/5)	1 (0.88)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	6 (6.90)	9 (9.78)
Relative Risk (RR) (95% CI)		1.4185 (0.5268, 3.8195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4891
Odds Ratio (OR) (95% CI)		1.4639 (0.4984, 4.2994)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4882
Risk Difference (RD) (95% CI)		0.0289 (-0.0519, 0.1096)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4836
Subjects with non-severe events (Maximum Grade 1/2)	5 (5.75)	9 (9.78)
Relative Risk (RR) (95% CI)		1.7022 (0.5938, 4.8798)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3222
Odds Ratio (OR) (95% CI)		1.7783 (0.5716, 5.5327)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3202

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Risk Difference (RD) (95% CI)		0.0404 (-0.0376, 0.1183)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3103
Subjects with severe events (Maximum Grade 3/4/5)	1 (1.15)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	2 (2.30)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	4 (12.90)	3 (11.54)
Relative Risk (RR) (95% CI)		0.8942 (0.2198, 3.6382)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8759
Odds Ratio (OR) (95% CI)		0.8804 (0.1783, 4.3474)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8758
Risk Difference (RD) (95% CI)		-0.0136 (-0.1840, 0.1567)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8752
Subjects with non-severe events (Maximum Grade 1/2)	3 (9.68)	3 (11.54)
Relative Risk (RR) (95% CI)		1.1923 (0.2626, 5.4137)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8198
Odds Ratio (OR) (95% CI)		1.2174 (0.2240, 6.6154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8198

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Risk Difference (RD) (95% CI)		0.0186 (-0.1424, 0.1796)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8207
Subjects with severe events (Maximum Grade 3/4/5)	1 (3.23)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	1 (3.23)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	9 (5.26)	13 (7.65)
Relative Risk (RR) (95% CI)		1.4529 (0.6380, 3.3087)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3736
Odds Ratio (OR) (95% CI)		1.4904 (0.6196, 3.5854)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3729
Risk Difference (RD) (95% CI)		0.0238 (-0.0283, 0.0760)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3700
Subjects with non-severe events (Maximum Grade 1/2)	8 (4.68)	13 (7.65)
Relative Risk (RR) (95% CI)		1.6346 (0.6953, 3.8425)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2599
Odds Ratio (OR) (95% CI)		1.6871 (0.6807, 4.1812)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2587

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Risk Difference (RD) (95% CI)		0.0297 (-0.0213, 0.0807)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2536
Subjects with severe events (Maximum Grade 3/4/5)	1 (0.58)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	1 (0.58)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	0	2 (11.76)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.1176 (-0.0355, 0.2708)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1322
Subjects with non-severe events (Maximum Grade 1/2)	0	2 (11.76)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Risk Difference (RD) (95% CI)		0.1176 (-0.0355, 0.2708)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1322
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	13 (7.14)	14 (7.91)
Relative Risk (RR) (95% CI)		1.1073 (0.5358, 2.2887)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7831
Odds Ratio (OR) (95% CI)		1.1166 (0.5093, 2.4479)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7831
Risk Difference (RD) (95% CI)		0.0077 (-0.0469, 0.0623)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7831
Subjects with non-severe events (Maximum Grade 1/2)	11 (6.04)	14 (7.91)
Relative Risk (RR) (95% CI)		1.3087 (0.6107, 2.8042)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4890
Odds Ratio (OR) (95% CI)		1.3352 (0.5891, 3.0265)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4887

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Risk Difference (RD) (95% CI)		0.0187 (-0.0341, 0.0714)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4879
Subjects with severe events (Maximum Grade 3/4/5)	2 (1.10)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	2 (1.10)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	9 (7.56)	11 (9.48)
Relative Risk (RR) (95% CI)		1.2538 (0.5397, 2.9131)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5989
Odds Ratio (OR) (95% CI)		1.2804 (0.5100, 3.2150)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5987
Risk Difference (RD) (95% CI)		0.0192 (-0.0522, 0.0906)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5983
Subjects with non-severe events (Maximum Grade 1/2)	7 (5.88)	11 (9.48)
Relative Risk (RR) (95% CI)		1.6121 (0.6473, 4.0148)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3050
Odds Ratio (OR) (95% CI)		1.6762 (0.6264, 4.4855)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3037

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- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Risk Difference (RD) (95% CI)		0.0360 (-0.0320, 0.1040)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2997
Subjects with severe events (Maximum Grade 3/4/5)	2 (1.68)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	1 (0.84)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	4 (4.82)	5 (6.25)
Relative Risk (RR) (95% CI)		1.2969 (0.3612, 4.6570)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6902
Odds Ratio (OR) (95% CI)		1.3167 (0.3406, 5.0902)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6901
Risk Difference (RD) (95% CI)		0.0143 (-0.0560, 0.0846)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6898
Subjects with non-severe events (Maximum Grade 1/2)	4 (4.82)	5 (6.25)
Relative Risk (RR) (95% CI)		1.2969 (0.3612, 4.6570)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6902
Odds Ratio (OR) (95% CI)		1.3167 (0.3406, 5.0902)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6901

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Risk Difference (RD) (95% CI)		0.0143 (-0.0560, 0.0846)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6898
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	1 (1.20)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	7 (7.69)	8 (9.20)
Relative Risk (RR) (95% CI)		1.1954 (0.4528, 3.1562)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7186
Odds Ratio (OR) (95% CI)		1.2152 (0.4211, 3.5070)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7185
Risk Difference (RD) (95% CI)		0.0150 (-0.0667, 0.0968)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7186
Subjects with non-severe events (Maximum Grade 1/2)	5 (5.49)	8 (9.20)
Relative Risk (RR) (95% CI)		1.6736 (0.5695, 4.9183)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3491
Odds Ratio (OR) (95% CI)		1.7418 (0.5469, 5.5470)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3478

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Risk Difference (RD) (95% CI)		0.0370 (-0.0397, 0.1137)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3441
Subjects with severe events (Maximum Grade 3/4/5)	2 (2.20)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	6 (5.41)	8 (7.34)
Relative Risk (RR) (95% CI)		1.3578 (0.4872, 3.7842)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5586
Odds Ratio (OR) (95% CI)		1.3861 (0.4646, 4.1359)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5583
Risk Difference (RD) (95% CI)		0.0193 (-0.0452, 0.0839)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5570
Subjects with non-severe events (Maximum Grade 1/2)	6 (5.41)	8 (7.34)
Relative Risk (RR) (95% CI)		1.3578 (0.4872, 3.7842)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5586
Odds Ratio (OR) (95% CI)		1.3861 (0.4646, 4.1359)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5583

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Risk Difference (RD) (95% CI)		0.0193 (-0.0452, 0.0839)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5570
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	2 (1.80)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.5.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Creatine Kinase Elevation Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.4965
Age at screening (<18 years vs. ≥18 years)	0.0722
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.3307
Sex (Male vs. Female)	0.4151
Region (North America vs. Rest of the World)	0.8831

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.6.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Creatine Kinase Elevation Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with non-severe events (Maximum Grade 1/2)	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.4373
Age at screening (<18 years vs. ≥18 years)	0.0672
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.3505
Sex (Male vs. Female)	0.3638
Region (North America vs. Rest of the World)	0.7886

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.6.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Creatine Kinase Elevation Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with severe events (Maximum Grade 3/4/5)	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.6.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Creatine Kinase Elevation Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with serious events	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	16 (14.04)	13 (12.87)
Relative Risk (RR) (95% CI)		0.9171 (0.4641, 1.8121)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8033
Odds Ratio (OR) (95% CI)		0.9048 (0.4121, 1.9866)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8032
Risk Difference (RD) (95% CI)		-0.0116 (-0.1029, 0.0796)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8027
Subjects with non-severe events (Maximum Grade 1/2)	15 (13.16)	13 (12.87)
Relative Risk (RR) (95% CI)		0.9782 (0.4893, 1.9556)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9503
Odds Ratio (OR) (95% CI)		0.9750 (0.4397, 2.1618)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9503

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- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Risk Difference (RD) (95% CI)		-0.0029 (-0.0930, 0.0872)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9503
Subjects with severe events (Maximum Grade 3/4/5)	1 (0.88)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	8 (9.20)	5 (5.43)
Relative Risk (RR) (95% CI)		0.5910 (0.2011, 1.7373)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3391
Odds Ratio (OR) (95% CI)		0.5675 (0.1782, 1.8070)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3377
Risk Difference (RD) (95% CI)		-0.0376 (-0.1140, 0.0388)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3345
Subjects with non-severe events (Maximum Grade 1/2)	8 (9.20)	5 (5.43)
Relative Risk (RR) (95% CI)		0.5910 (0.2011, 1.7373)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3391
Odds Ratio (OR) (95% CI)		0.5675 (0.1782, 1.8070)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3377

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Risk Difference (RD) (95% CI)		-0.0376 (-0.1140, 0.0388)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3345
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	1 (1.15)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	3 (9.68)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0968 (-0.2008, 0.0073)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0684
Subjects with non-severe events (Maximum Grade 1/2)	3 (9.68)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Risk Difference (RD) (95% CI)		-0.0968 (-0.2008, 0.0073)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0684
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	1 (3.23)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	21 (12.28)	18 (10.59)
Relative Risk (RR) (95% CI)		0.8622 (0.4766, 1.5596)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6239
Odds Ratio (OR) (95% CI)		0.8459 (0.4334, 1.6510)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6237
Risk Difference (RD) (95% CI)		-0.0169 (-0.0844, 0.0506)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6232
Subjects with non-severe events (Maximum Grade 1/2)	20 (11.70)	18 (10.59)
Relative Risk (RR) (95% CI)		0.9053 (0.4967, 1.6501)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7453
Odds Ratio (OR) (95% CI)		0.8941 (0.4550, 1.7567)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7453

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Risk Difference (RD) (95% CI)		-0.0111 (-0.0779, 0.0557)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7451
Subjects with severe events (Maximum Grade 3/4/5)	1 (0.58)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	1 (5.26)	2 (11.76)
Relative Risk (RR) (95% CI)		2.2353 (0.2220, 22.5093)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4948
Odds Ratio (OR) (95% CI)		2.4000 (0.1977, 29.1311)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4919
Risk Difference (RD) (95% CI)		0.0650 (-0.1181, 0.2481)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4865
Subjects with non-severe events (Maximum Grade 1/2)	1 (5.26)	2 (11.76)
Relative Risk (RR) (95% CI)		2.2353 (0.2220, 22.5093)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4948
Odds Ratio (OR) (95% CI)		2.4000 (0.1977, 29.1311)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4919

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Risk Difference (RD) (95% CI)		0.0650 (-0.1181, 0.2481)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4865
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	23 (12.64)	16 (9.04)
Relative Risk (RR) (95% CI)		0.7153 (0.3912, 1.3080)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2766
Odds Ratio (OR) (95% CI)		0.6870 (0.3499, 1.3488)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2754
Risk Difference (RD) (95% CI)		-0.0360 (-0.1001, 0.0282)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2716
Subjects with non-severe events (Maximum Grade 1/2)	22 (12.09)	16 (9.04)
Relative Risk (RR) (95% CI)		0.7478 (0.4064, 1.3761)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3503
Odds Ratio (OR) (95% CI)		0.7228 (0.3661, 1.4268)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3494

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Risk Difference (RD) (95% CI)		-0.0305 (-0.0939, 0.0330)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3465
Subjects with severe events (Maximum Grade 3/4/5)	1 (0.55)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	1 (0.55)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	16 (13.45)	14 (12.07)
Relative Risk (RR) (95% CI)		0.8976 (0.4593, 1.7544)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7521
Odds Ratio (OR) (95% CI)		0.8836 (0.4100, 1.9040)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7520
Risk Difference (RD) (95% CI)		-0.0138 (-0.0990, 0.0715)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7517
Subjects with non-severe events (Maximum Grade 1/2)	15 (12.61)	14 (12.07)
Relative Risk (RR) (95% CI)		0.9575 (0.4841, 1.8937)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9006
Odds Ratio (OR) (95% CI)		0.9516 (0.4372, 2.0716)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9006

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- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Risk Difference (RD) (95% CI)		-0.0054 (-0.0894, 0.0787)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9006
Subjects with severe events (Maximum Grade 3/4/5)	1 (0.84)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	1 (0.84)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	8 (9.64)	4 (5.00)
Relative Risk (RR) (95% CI)		0.5188 (0.1626, 1.6552)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2676
Odds Ratio (OR) (95% CI)		0.4934 (0.1425, 1.7083)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2649
Risk Difference (RD) (95% CI)		-0.0464 (-0.1258, 0.0331)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2525
Subjects with non-severe events (Maximum Grade 1/2)	8 (9.64)	4 (5.00)
Relative Risk (RR) (95% CI)		0.5188 (0.1626, 1.6552)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2676
Odds Ratio (OR) (95% CI)		0.4934 (0.1425, 1.7083)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2649

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Risk Difference (RD) (95% CI)		-0.0464 (-0.1258, 0.0331)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2525
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	10 (10.99)	7 (8.05)
Relative Risk (RR) (95% CI)		0.7322 (0.2918, 1.8374)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5067
Odds Ratio (OR) (95% CI)		0.7088 (0.2571, 1.9539)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5058
Risk Difference (RD) (95% CI)		-0.0294 (-0.1154, 0.0566)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5024
Subjects with non-severe events (Maximum Grade 1/2)	10 (10.99)	7 (8.05)
Relative Risk (RR) (95% CI)		0.7322 (0.2918, 1.8374)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5067
Odds Ratio (OR) (95% CI)		0.7088 (0.2571, 1.9539)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5058

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Risk Difference (RD) (95% CI)		-0.0294 (-0.1154, 0.0566)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5024
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	1 (1.10)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	14 (12.61)	11 (10.09)
Relative Risk (RR) (95% CI)		0.8001 (0.3802, 1.6840)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5570
Odds Ratio (OR) (95% CI)		0.7777 (0.3364, 1.7980)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5566
Risk Difference (RD) (95% CI)		-0.0252 (-0.1089, 0.0585)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5552
Subjects with non-severe events (Maximum Grade 1/2)	13 (11.71)	11 (10.09)
Relative Risk (RR) (95% CI)		0.8617 (0.4037, 1.8392)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7004
Odds Ratio (OR) (95% CI)		0.8462 (0.3615, 1.9804)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7002

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Risk Difference (RD) (95% CI)		-0.0162 (-0.0985, 0.0661)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6997
Subjects with severe events (Maximum Grade 3/4/5)	1 (0.90)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.6.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Rash Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any Treatment-emergent Rash Events	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.2000
Age at screening (<18 years vs. ≥18 years)	0.9797
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.6514
Sex (Male vs. Female)	0.2358
Region (North America vs. Rest of the World)	0.3487

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.7.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Rash Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with non-severe events (Maximum Grade 1/2)	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.2000
Age at screening (<18 years vs. ≥18 years)	0.9797
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.6514
Sex (Male vs. Female)	0.2358
Region (North America vs. Rest of the World)	0.3487

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.7.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Rash Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with severe events (Maximum Grade 3/4/5)	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.7.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Rash Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with serious events	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Subjects with any Treatment-emergent Rash Events	9 (7.89)	13 (12.87)
Relative Risk (RR) (95% CI)		1.6304 (0.7278, 3.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2349
Odds Ratio (OR) (95% CI)		1.7235 (0.7036, 4.2216)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2337
Risk Difference (RD) (95% CI)		0.0498 (-0.0322, 0.1317)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2340
Subjects with non-severe events (Maximum Grade 1/2)	9 (7.89)	13 (12.87)
Relative Risk (RR) (95% CI)		1.6304 (0.7278, 3.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2349
Odds Ratio (OR) (95% CI)		1.7235 (0.7036, 4.2216)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2337

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Risk Difference (RD) (95% CI)		0.0498 (-0.0322, 0.1317)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2340
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Subjects with any Treatment-emergent Rash Events	6 (6.90)	4 (4.35)
Relative Risk (RR) (95% CI)		0.6304 (0.1841, 2.1584)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4625
Odds Ratio (OR) (95% CI)		0.6136 (0.1671, 2.2531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4618
Risk Difference (RD) (95% CI)		-0.0255 (-0.0931, 0.0421)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4600
Subjects with non-severe events (Maximum Grade 1/2)	6 (6.90)	4 (4.35)
Relative Risk (RR) (95% CI)		0.6304 (0.1841, 2.1584)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4625
Odds Ratio (OR) (95% CI)		0.6136 (0.1671, 2.2531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4618

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Risk Difference (RD) (95% CI)		-0.0255 (-0.0931, 0.0421)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4600
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with any Treatment-emergent Rash Events	1 (3.23)	1 (3.85)
Relative Risk (RR) (95% CI)		1.1923 (0.0784, 18.1424)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8992
Odds Ratio (OR) (95% CI)		1.2000 (0.0714, 20.1759)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8992
Risk Difference (RD) (95% CI)		0.0062 (-0.0904, 0.1028)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8998
Subjects with non-severe events (Maximum Grade 1/2)	1 (3.23)	1 (3.85)
Relative Risk (RR) (95% CI)		1.1923 (0.0784, 18.1424)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8992
Odds Ratio (OR) (95% CI)		1.2000 (0.0714, 20.1759)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8992

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Risk Difference (RD) (95% CI)		0.0062 (-0.0904, 0.1028)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8998
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any Treatment-emergent Rash Events	14 (8.19)	16 (9.41)
Relative Risk (RR) (95% CI)		1.1496 (0.5794, 2.2808)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6901
Odds Ratio (OR) (95% CI)		1.1651 (0.5499, 2.4689)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6900
Risk Difference (RD) (95% CI)		0.0122 (-0.0479, 0.0724)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6897
Subjects with non-severe events (Maximum Grade 1/2)	14 (8.19)	16 (9.41)
Relative Risk (RR) (95% CI)		1.1496 (0.5794, 2.2808)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6901
Odds Ratio (OR) (95% CI)		1.1651 (0.5499, 2.4689)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6900

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Risk Difference (RD) (95% CI)		0.0122 (-0.0479, 0.0724)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6897
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with any Treatment-emergent Rash Events	2 (10.53)	3 (17.65)
Relative Risk (RR) (95% CI)		1.6765 (0.3171, 8.8635)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5431
Odds Ratio (OR) (95% CI)		1.8214 (0.2660, 12.4730)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5413
Risk Difference (RD) (95% CI)		0.0712 (-0.1566, 0.2990)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5401
Subjects with non-severe events (Maximum Grade 1/2)	2 (10.53)	3 (17.65)
Relative Risk (RR) (95% CI)		1.6765 (0.3171, 8.8635)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5431
Odds Ratio (OR) (95% CI)		1.8214 (0.2660, 12.4730)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5413

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Risk Difference (RD) (95% CI)		0.0712 (-0.1566, 0.2990)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5401
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with any Treatment-emergent Rash Events	13 (7.14)	14 (7.91)
Relative Risk (RR) (95% CI)		1.1073 (0.5358, 2.2887)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7831
Odds Ratio (OR) (95% CI)		1.1166 (0.5093, 2.4479)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7831
Risk Difference (RD) (95% CI)		0.0077 (-0.0469, 0.0623)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7831
Subjects with non-severe events (Maximum Grade 1/2)	13 (7.14)	14 (7.91)
Relative Risk (RR) (95% CI)		1.1073 (0.5358, 2.2887)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7831
Odds Ratio (OR) (95% CI)		1.1166 (0.5093, 2.4479)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7831

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Risk Difference (RD) (95% CI)		0.0077 (-0.0469, 0.0623)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7831
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Subjects with any Treatment-emergent Rash Events	10 (8.40)	8 (6.90)
Relative Risk (RR) (95% CI)		0.8207 (0.3357, 2.0062)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6648
Odds Ratio (OR) (95% CI)		0.8074 (0.3070, 2.1236)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6646
Risk Difference (RD) (95% CI)		-0.0151 (-0.0830, 0.0528)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6636
Subjects with non-severe events (Maximum Grade 1/2)	10 (8.40)	8 (6.90)
Relative Risk (RR) (95% CI)		0.8207 (0.3357, 2.0062)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6648
Odds Ratio (OR) (95% CI)		0.8074 (0.3070, 2.1236)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6646

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Risk Difference (RD) (95% CI)		-0.0151 (-0.0830, 0.0528)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6636
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Subjects with any Treatment-emergent Rash Events	5 (6.02)	9 (11.25)
Relative Risk (RR) (95% CI)		1.8675 (0.6540, 5.3324)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2433
Odds Ratio (OR) (95% CI)		1.9775 (0.6327, 6.1800)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2409
Risk Difference (RD) (95% CI)		0.0523 (-0.0338, 0.1384)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2342
Subjects with non-severe events (Maximum Grade 1/2)	5 (6.02)	9 (11.25)
Relative Risk (RR) (95% CI)		1.8675 (0.6540, 5.3324)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2433
Odds Ratio (OR) (95% CI)		1.9775 (0.6327, 6.1800)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2409

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Risk Difference (RD) (95% CI)		0.0523 (-0.0338, 0.1384)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2342
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Subjects with any Treatment-emergent Rash Events	4 (4.40)	7 (8.05)
Relative Risk (RR) (95% CI)		1.8305 (0.5553, 6.0338)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3205
Odds Ratio (OR) (95% CI)		1.9031 (0.5369, 6.7459)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3189
Risk Difference (RD) (95% CI)		0.0365 (-0.0345, 0.1075)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3136
Subjects with non-severe events (Maximum Grade 1/2)	4 (4.40)	7 (8.05)
Relative Risk (RR) (95% CI)		1.8305 (0.5553, 6.0338)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3205
Odds Ratio (OR) (95% CI)		1.9031 (0.5369, 6.7459)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3189

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- A subject with multiple events within a category is counted only once in that category.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Risk Difference (RD) (95% CI)		0.0365 (-0.0345, 0.1075)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3136
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Subjects with any Treatment-emergent Rash Events	11 (9.91)	10 (9.17)
Relative Risk (RR) (95% CI)		0.9258 (0.4100, 2.0906)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8528
Odds Ratio (OR) (95% CI)		0.9183 (0.3732, 2.2593)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8528
Risk Difference (RD) (95% CI)		-0.0074 (-0.0850, 0.0703)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8527
Subjects with non-severe events (Maximum Grade 1/2)	11 (9.91)	10 (9.17)
Relative Risk (RR) (95% CI)		0.9258 (0.4100, 2.0906)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8528
Odds Ratio (OR) (95% CI)		0.9183 (0.3732, 2.2593)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8528

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Risk Difference (RD) (95% CI)		-0.0074 (-0.0850, 0.0703)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8527
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.7.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.8.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Cataract Events
Safety Set

	P-value for Interaction Based on Relative Risk

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.8.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.8.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.8.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.8.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.8.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.8.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.8.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.8.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.8.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.8.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Hypoglycemia Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any Treatment-emergent Hypoglycemia Events	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	0.3127
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	>0.9999
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.9.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Hypoglycemia Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with non-severe events (Maximum Grade 1/2)	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	0.3561
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	>0.9999
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.9.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Hypoglycemia Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with severe events (Maximum Grade 3/4/5)	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.9.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Hypoglycemia Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with serious events	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

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Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	5 (4.39)	3 (2.97)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	5 (4.39)	2 (1.98)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	1 (0.99)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	2 (2.30)	2 (2.17)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	2 (2.30)	2 (2.17)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	1 (3.23)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0323 (-0.0945, 0.0299)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3094
Subjects with non-severe events (Maximum Grade 1/2)	1 (3.23)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Risk Difference (RD) (95% CI)		-0.0323 (-0.0945, 0.0299)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3094
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	6 (3.51)	5 (2.94)
Relative Risk (RR) (95% CI)		0.8382 (0.2608, 2.6945)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7671
Odds Ratio (OR) (95% CI)		0.8333 (0.2494, 2.7842)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7670
Risk Difference (RD) (95% CI)		-0.0057 (-0.0432, 0.0318)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7667
Subjects with non-severe events (Maximum Grade 1/2)	6 (3.51)	4 (2.35)
Relative Risk (RR) (95% CI)		0.6706 (0.1927, 2.3341)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5300
Odds Ratio (OR) (95% CI)		0.6627 (0.1836, 2.3914)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5297

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Risk Difference (RD) (95% CI)		-0.0116 (-0.0473, 0.0242)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5266
Subjects with severe events (Maximum Grade 3/4/5)	0	1 (0.59)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	7 (3.85)	5 (2.82)
Relative Risk (RR) (95% CI)		0.7345 (0.2375, 2.2710)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5921
Odds Ratio (OR) (95% CI)		0.7267 (0.2263, 2.3340)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5918
Risk Difference (RD) (95% CI)		-0.0102 (-0.0473, 0.0269)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5895
Subjects with non-severe events (Maximum Grade 1/2)	7 (3.85)	4 (2.26)
Relative Risk (RR) (95% CI)		0.5876 (0.1751, 1.9722)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3894
Odds Ratio (OR) (95% CI)		0.5780 (0.1662, 2.0101)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3887

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Risk Difference (RD) (95% CI)		-0.0159 (-0.0514, 0.0196)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3811
Subjects with severe events (Maximum Grade 3/4/5)	0	1 (0.56)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	5 (4.20)	3 (2.59)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	5 (4.20)	3 (2.59)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	2 (2.41)	2 (2.50)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	2 (2.41)	1 (1.25)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	1 (1.25)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	5 (5.49)	3 (3.45)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	5 (5.49)	3 (3.45)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	2 (1.80)	2 (1.83)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	2 (1.80)	1 (0.92)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	1 (0.92)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.9.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Neuropsychiatric Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any Treatment-emergent Neuropsychiatric Events	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.2950
Age at screening (<18 years vs. ≥18 years)	0.0672
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.2431
Sex (Male vs. Female)	0.5753
Region (North America vs. Rest of the World)	0.2854

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.10.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Neuropsychiatric Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with non-severe events (Maximum Grade 1/2)	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.4539
Age at screening (<18 years vs. ≥18 years)	0.0630
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.6616
Sex (Male vs. Female)	0.2520
Region (North America vs. Rest of the World)	0.3165

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.10.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Neuropsychiatric Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with severe events (Maximum Grade 3/4/5)	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.10.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Neuropsychiatric Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with serious events	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	17 (14.91)	7 (6.93)
Relative Risk (RR) (95% CI)		0.4648 (0.2010, 1.0749)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0733
Odds Ratio (OR) (95% CI)		0.4249 (0.1685, 1.0713)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0697
Risk Difference (RD) (95% CI)		-0.0798 (-0.1618, 0.0022)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0565
Subjects with non-severe events (Maximum Grade 1/2)	14 (12.28)	6 (5.94)
Relative Risk (RR) (95% CI)		0.4837 (0.1931, 1.2115)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1211
Odds Ratio (OR) (95% CI)		0.4511 (0.1665, 1.2223)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1175

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Risk Difference (RD) (95% CI)		-0.0634 (-0.1393, 0.0125)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1014
Subjects with severe events (Maximum Grade 3/4/5)	3 (2.63)	1 (0.99)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	2 (1.75)	1 (0.99)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	11 (12.64)	10 (10.87)
Relative Risk (RR) (95% CI)		0.8597 (0.3845, 1.9222)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7127
Odds Ratio (OR) (95% CI)		0.8426 (0.3387, 2.0963)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7126
Risk Difference (RD) (95% CI)		-0.0177 (-0.1122, 0.0767)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7128
Subjects with non-severe events (Maximum Grade 1/2)	11 (12.64)	9 (9.78)
Relative Risk (RR) (95% CI)		0.7737 (0.3371, 1.7757)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5450
Odds Ratio (OR) (95% CI)		0.7492 (0.2943, 1.9069)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5446

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Risk Difference (RD) (95% CI)		-0.0286 (-0.1211, 0.0639)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5445
Subjects with severe events (Maximum Grade 3/4/5)	0	1 (1.09)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	2 (2.17)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

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- A subject with multiple events within a category is counted only once in that category.
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- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	2 (6.45)	4 (15.38)
Relative Risk (RR) (95% CI)		2.3846 (0.4741, 11.9940)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2917
Odds Ratio (OR) (95% CI)		2.6364 (0.4421, 15.7202)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2873
Risk Difference (RD) (95% CI)		0.0893 (-0.0741, 0.2528)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2841
Subjects with non-severe events (Maximum Grade 1/2)	2 (6.45)	4 (15.38)
Relative Risk (RR) (95% CI)		2.3846 (0.4741, 11.9940)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2917
Odds Ratio (OR) (95% CI)		2.6364 (0.4421, 15.7202)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2873

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- A subject with multiple events within a category is counted only once in that category.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Risk Difference (RD) (95% CI)		0.0893 (-0.0741, 0.2528)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2841
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	26 (15.20)	13 (7.65)
Relative Risk (RR) (95% CI)		0.5029 (0.2676, 0.9453)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0328
Odds Ratio (OR) (95% CI)		0.4618 (0.2286, 0.9327)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0312
Risk Difference (RD) (95% CI)		-0.0756 (-0.1426, -0.0086)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0271
Subjects with non-severe events (Maximum Grade 1/2)	23 (13.45)	11 (6.47)
Relative Risk (RR) (95% CI)		0.4811 (0.2422, 0.9557)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0367
Odds Ratio (OR) (95% CI)		0.4452 (0.2097, 0.9449)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0351

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Risk Difference (RD) (95% CI)		-0.0698 (-0.1329, -0.0067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0302
Subjects with severe events (Maximum Grade 3/4/5)	3 (1.75)	2 (1.18)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	2 (1.17)	3 (1.76)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once in that category.
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- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	1 (5.26)	2 (11.76)
Relative Risk (RR) (95% CI)		2.2353 (0.2220, 22.5093)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4948
Odds Ratio (OR) (95% CI)		2.4000 (0.1977, 29.1311)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4919
Risk Difference (RD) (95% CI)		0.0650 (-0.1181, 0.2481)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4865
Subjects with non-severe events (Maximum Grade 1/2)	1 (5.26)	1 (5.88)
Relative Risk (RR) (95% CI)		1.1176 (0.0756, 16.5220)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9355
Odds Ratio (OR) (95% CI)		1.1250 (0.0649, 19.4963)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9355

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Risk Difference (RD) (95% CI)		0.0062 (-0.1441, 0.1565)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9356
Subjects with severe events (Maximum Grade 3/4/5)	0	1 (5.88)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	1 (5.88)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

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- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	27 (14.84)	15 (8.47)
Relative Risk (RR) (95% CI)		0.5712 (0.3147, 1.0370)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0657
Odds Ratio (OR) (95% CI)		0.5316 (0.2724, 1.0372)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0639
Risk Difference (RD) (95% CI)		-0.0636 (-0.1296, 0.0023)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0587
Subjects with non-severe events (Maximum Grade 1/2)	24 (13.19)	14 (7.91)
Relative Risk (RR) (95% CI)		0.5998 (0.3208, 1.1215)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1094
Odds Ratio (OR) (95% CI)		0.5654 (0.2823, 1.1324)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1076

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- A subject with multiple events within a category is counted only once in that category.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Risk Difference (RD) (95% CI)		-0.0528 (-0.1160, 0.0105)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1018
Subjects with severe events (Maximum Grade 3/4/5)	3 (1.65)	1 (0.56)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	2 (1.10)	2 (1.13)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	17 (14.29)	9 (7.76)
Relative Risk (RR) (95% CI)		0.5431 (0.2524, 1.1688)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1185
Odds Ratio (OR) (95% CI)		0.5047 (0.2152, 1.1834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1158
Risk Difference (RD) (95% CI)		-0.0653 (-0.1448, 0.0142)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1077
Subjects with non-severe events (Maximum Grade 1/2)	16 (13.45)	7 (6.03)
Relative Risk (RR) (95% CI)		0.4488 (0.1917, 1.0507)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0649
Odds Ratio (OR) (95% CI)		0.4134 (0.1634, 1.0458)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0621

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Risk Difference (RD) (95% CI)		-0.0741 (-0.1492, 0.0010)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0530
Subjects with severe events (Maximum Grade 3/4/5)	1 (0.84)	2 (1.72)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	1 (0.84)	3 (2.59)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	11 (13.25)	8 (10.00)
Relative Risk (RR) (95% CI)		0.7545 (0.3201, 1.7785)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5197
Odds Ratio (OR) (95% CI)		0.7273 (0.2764, 1.9138)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5189
Risk Difference (RD) (95% CI)		-0.0325 (-0.1307, 0.0657)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5162
Subjects with non-severe events (Maximum Grade 1/2)	9 (10.84)	8 (10.00)
Relative Risk (RR) (95% CI)		0.9222 (0.3744, 2.2717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8603
Odds Ratio (OR) (95% CI)		0.9136 (0.3340, 2.4986)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8602

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- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Risk Difference (RD) (95% CI)		-0.0084 (-0.1022, 0.0854)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8601
Subjects with severe events (Maximum Grade 3/4/5)	2 (2.41)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	1 (1.20)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	14 (15.38)	11 (12.64)
Relative Risk (RR) (95% CI)		0.8218 (0.3949, 1.7105)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5998
Odds Ratio (OR) (95% CI)		0.7961 (0.3399, 1.8642)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5993
Risk Difference (RD) (95% CI)		-0.0274 (-0.1293, 0.0744)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5979
Subjects with non-severe events (Maximum Grade 1/2)	13 (14.29)	10 (11.49)
Relative Risk (RR) (95% CI)		0.8046 (0.3724, 1.7382)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5801
Odds Ratio (OR) (95% CI)		0.7792 (0.3224, 1.8833)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5796

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Risk Difference (RD) (95% CI)		-0.0279 (-0.1262, 0.0704)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5778
Subjects with severe events (Maximum Grade 3/4/5)	1 (1.10)	1 (1.15)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	1 (1.15)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	14 (12.61)	6 (5.50)
Relative Risk (RR) (95% CI)		0.4364 (0.1741, 1.0942)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0771
Odds Ratio (OR) (95% CI)		0.4036 (0.1491, 1.0925)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0741
Risk Difference (RD) (95% CI)		-0.0711 (-0.1462, 0.0041)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0638
Subjects with non-severe events (Maximum Grade 1/2)	12 (10.81)	5 (4.59)
Relative Risk (RR) (95% CI)		0.4243 (0.1547, 1.1641)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0959
Odds Ratio (OR) (95% CI)		0.3966 (0.1348, 1.1667)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0930

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Risk Difference (RD) (95% CI)		-0.0622 (-0.1321, 0.0076)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0808
Subjects with severe events (Maximum Grade 3/4/5)	2 (1.80)	1 (0.92)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	2 (1.80)	2 (1.83)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.10.2
Study VX20-121-102: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.11.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Death
Safety Set

	P-value for Interaction Based on Relative Risk

No data met the criteria for this table.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.11.2
Study VX20-121-102: Summary of Death by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.11.2
Study VX20-121-102: Summary of Death by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.11.2
Study VX20-121-102: Summary of Death by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.11.2
Study VX20-121-102: Summary of Death by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.11.2
Study VX20-121-102: Summary of Death by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.11.2
Study VX20-121-102: Summary of Death by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.11.2
Study VX20-121-102: Summary of Death by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.11.2
Study VX20-121-102: Summary of Death by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.11.2
Study VX20-121-102: Summary of Death by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.11.2
Study VX20-121-102: Summary of Death by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Treatment-emergent Infective Pulmonary Exacerbation Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.8193
Age at screening (<18 years vs. ≥18 years)	0.5205
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.3192
Sex (Male vs. Female)	0.4849
Region (North America vs. Rest of the World)	0.4279

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.12.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Treatment-emergent Infective Pulmonary Exacerbation Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with non-severe events (Maximum Grade 1/2)	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.6060
Age at screening (<18 years vs. ≥18 years)	0.3020
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.4288
Sex (Male vs. Female)	0.3633
Region (North America vs. Rest of the World)	0.5979

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.12.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Treatment-emergent Infective Pulmonary Exacerbation Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with severe events (Maximum Grade 3/4/5)	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	0.3895
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.3920
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.0737

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.12.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Treatment-emergent Infective Pulmonary Exacerbation Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with serious events	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.3753
Age at screening (<18 years vs. ≥18 years)	0.2418
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.0781
Sex (Male vs. Female)	0.8800
Region (North America vs. Rest of the World)	0.3209

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	44 (38.60)	33 (32.67)
Relative Risk (RR) (95% CI)		0.8465 (0.5887, 1.2174)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3687
Odds Ratio (OR) (95% CI)		0.7721 (0.4404, 1.3534)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3664
Risk Difference (RD) (95% CI)		-0.0592 (-0.1871, 0.0686)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3640
Subjects with non-severe events (Maximum Grade 1/2)	37 (32.46)	32 (31.68)
Relative Risk (RR) (95% CI)		0.9762 (0.6609, 1.4419)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9036
Odds Ratio (OR) (95% CI)		0.9651 (0.5437, 1.7134)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9036

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Risk Difference (RD) (95% CI)		-0.0077 (-0.1327, 0.1172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9035
Subjects with severe events (Maximum Grade 3/4/5)	7 (6.14)	1 (0.99)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	15 (13.16)	5 (4.95)
Relative Risk (RR) (95% CI)		0.3762 (0.1418, 0.9985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0497

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Odds Ratio (OR) (95% CI)		0.3438 (0.1203, 0.9826)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0463
Risk Difference (RD) (95% CI)		-0.0821 (-0.1572, -0.0070)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0322

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	25 (28.74)	24 (26.09)
Relative Risk (RR) (95% CI)		0.9078 (0.5633, 1.4631)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6913
Odds Ratio (OR) (95% CI)		0.8753 (0.4536, 1.6891)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6913
Risk Difference (RD) (95% CI)		-0.0265 (-0.1572, 0.1043)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6913
Subjects with non-severe events (Maximum Grade 1/2)	23 (26.44)	20 (21.74)
Relative Risk (RR) (95% CI)		0.8223 (0.4876, 1.3868)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4632
Odds Ratio (OR) (95% CI)		0.7729 (0.3887, 1.5370)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4627

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Risk Difference (RD) (95% CI)		-0.0470 (-0.1722, 0.0783)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4623
Subjects with severe events (Maximum Grade 3/4/5)	2 (2.30)	4 (4.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	8 (9.20)	6 (6.52)
Relative Risk (RR) (95% CI)		0.7092 (0.2565, 1.9612)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5079

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- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Odds Ratio (OR) (95% CI)		0.6890 (0.2289, 2.0732)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5074
Risk Difference (RD) (95% CI)		-0.0267 (-0.1057, 0.0522)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5068

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	11 (35.48)	6 (23.08)
Relative Risk (RR) (95% CI)		0.6503 (0.2787, 1.5174)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3196
Odds Ratio (OR) (95% CI)		0.5455 (0.1690, 1.7610)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3108
Risk Difference (RD) (95% CI)		-0.1241 (-0.3577, 0.1096)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2980
Subjects with non-severe events (Maximum Grade 1/2)	9 (29.03)	4 (15.38)
Relative Risk (RR) (95% CI)		0.5299 (0.1843, 1.5237)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2386
Odds Ratio (OR) (95% CI)		0.4444 (0.1190, 1.6600)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2278

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Risk Difference (RD) (95% CI)		-0.1365 (-0.3481, 0.0751)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2061
Subjects with severe events (Maximum Grade 3/4/5)	2 (6.45)	2 (7.69)
Relative Risk (RR) (95% CI)		1.1923 (0.1802, 7.8875)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8552
Odds Ratio (OR) (95% CI)		1.2083 (0.1582, 9.2300)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8553
Risk Difference (RD) (95% CI)		0.0124 (-0.1216, 0.1465)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8561
Subjects with serious events	5 (16.13)	4 (15.38)
Relative Risk (RR) (95% CI)		0.9538 (0.2853, 3.1893)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9388

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Odds Ratio (OR) (95% CI)		0.9455 (0.2258, 3.9592)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9388
Risk Difference (RD) (95% CI)		-0.0074 (-0.1972, 0.1823)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9387

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	59 (34.50)	51 (30.00)
Relative Risk (RR) (95% CI)		0.8695 (0.6385, 1.1841)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3748
Odds Ratio (OR) (95% CI)		0.8136 (0.5162, 1.2823)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3741
Risk Difference (RD) (95% CI)		-0.0450 (-0.1441, 0.0541)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3732
Subjects with non-severe events (Maximum Grade 1/2)	52 (30.41)	48 (28.24)
Relative Risk (RR) (95% CI)		0.9285 (0.6676, 1.2914)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6594
Odds Ratio (OR) (95% CI)		0.9004 (0.5647, 1.4356)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6593

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Risk Difference (RD) (95% CI)		-0.0217 (-0.1183, 0.0749)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6592
Subjects with severe events (Maximum Grade 3/4/5)	7 (4.09)	3 (1.76)
Relative Risk (RR) (95% CI)		0.4311 (0.1134, 1.6394)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2170
Odds Ratio (OR) (95% CI)		0.4209 (0.1070, 1.6556)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2155
Risk Difference (RD) (95% CI)		-0.0233 (-0.0590, 0.0124)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2009
Subjects with serious events	18 (10.53)	7 (4.12)
Relative Risk (RR) (95% CI)		0.3912 (0.1677, 0.9123)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0298

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Odds Ratio (OR) (95% CI)		0.3650 (0.1483, 0.8983)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0283
Risk Difference (RD) (95% CI)		-0.0641 (-0.1189, -0.0092)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0220

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	7 (36.84)	3 (17.65)
Relative Risk (RR) (95% CI)		0.4790 (0.1466, 1.5646)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2229
Odds Ratio (OR) (95% CI)		0.3673 (0.0774, 1.7426)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2074
Risk Difference (RD) (95% CI)		-0.1920 (-0.4746, 0.0907)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1832
Subjects with non-severe events (Maximum Grade 1/2)	6 (31.58)	3 (17.65)
Relative Risk (RR) (95% CI)		0.5588 (0.1647, 1.8961)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3505
Odds Ratio (OR) (95% CI)		0.4643 (0.0958, 2.2500)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3407

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Risk Difference (RD) (95% CI)		-0.1393 (-0.4159, 0.1373)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3236
Subjects with severe events (Maximum Grade 3/4/5)	1 (5.26)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0526 (-0.1530, 0.0478)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3042
Subjects with serious events	4 (21.05)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.2105 (-0.3938, -0.0272)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0244

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	63 (34.62)	53 (29.94)
Relative Risk (RR) (95% CI)		0.8650 (0.6401, 1.1689)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3452
Odds Ratio (OR) (95% CI)		0.8073 (0.5181, 1.2580)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3443
Risk Difference (RD) (95% CI)		-0.0467 (-0.1433, 0.0499)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3431
Subjects with non-severe events (Maximum Grade 1/2)	55 (30.22)	49 (27.68)
Relative Risk (RR) (95% CI)		0.9161 (0.6621, 1.2675)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5967
Odds Ratio (OR) (95% CI)		0.8839 (0.5599, 1.3955)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5965

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Risk Difference (RD) (95% CI)		-0.0254 (-0.1191, 0.0684)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5961
Subjects with severe events (Maximum Grade 3/4/5)	8 (4.40)	4 (2.26)
Relative Risk (RR) (95% CI)		0.5141 (0.1576, 1.6769)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2701
Odds Ratio (OR) (95% CI)		0.5029 (0.1487, 1.7009)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2689
Risk Difference (RD) (95% CI)		-0.0214 (-0.0583, 0.0156)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2575
Subjects with serious events	19 (10.44)	10 (5.65)
Relative Risk (RR) (95% CI)		0.5412 (0.2589, 1.1312)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1026

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Odds Ratio (OR) (95% CI)		0.5137 (0.2319, 1.1382)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1008
Risk Difference (RD) (95% CI)		-0.0479 (-0.1038, 0.0081)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0934

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	38 (31.93)	34 (29.31)
Relative Risk (RR) (95% CI)		0.9179 (0.6242, 1.3497)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6631
Odds Ratio (OR) (95% CI)		0.8838 (0.5072, 1.5400)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6629
Risk Difference (RD) (95% CI)		-0.0262 (-0.1440, 0.0916)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6626
Subjects with non-severe events (Maximum Grade 1/2)	33 (27.73)	32 (27.59)
Relative Risk (RR) (95% CI)		0.9948 (0.6578, 1.5043)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9802
Odds Ratio (OR) (95% CI)		0.9928 (0.5605, 1.7585)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9802

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- [2] Odds ratio from 2x2 table.
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Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Risk Difference (RD) (95% CI)		-0.0014 (-0.1158, 0.1129)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9802
Subjects with severe events (Maximum Grade 3/4/5)	5 (4.20)	2 (1.72)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	11 (9.24)	5 (4.31)
Relative Risk (RR) (95% CI)		0.4663 (0.1672, 1.3006)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1449

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Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Odds Ratio (OR) (95% CI)		0.4423 (0.1487, 1.3152)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1423
Risk Difference (RD) (95% CI)		-0.0493 (-0.1132, 0.0145)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1298

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	32 (38.55)	23 (28.75)
Relative Risk (RR) (95% CI)		0.7457 (0.4807, 1.1568)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1902
Odds Ratio (OR) (95% CI)		0.6431 (0.3339, 1.2388)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1869
Risk Difference (RD) (95% CI)		-0.0980 (-0.2423, 0.0462)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1827
Subjects with non-severe events (Maximum Grade 1/2)	28 (33.73)	20 (25.00)
Relative Risk (RR) (95% CI)		0.7411 (0.4564, 1.2033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2257
Odds Ratio (OR) (95% CI)		0.6548 (0.3315, 1.2931)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2226

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Risk Difference (RD) (95% CI)		-0.0873 (-0.2265, 0.0518)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2184
Subjects with severe events (Maximum Grade 3/4/5)	4 (4.82)	3 (3.75)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	12 (14.46)	6 (7.50)
Relative Risk (RR) (95% CI)		0.5188 (0.2045, 1.3156)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1669

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Odds Ratio (OR) (95% CI)		0.4797 (0.1708, 1.3473)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1633
Risk Difference (RD) (95% CI)		-0.0696 (-0.1647, 0.0256)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1518

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	32 (35.16)	29 (33.33)
Relative Risk (RR) (95% CI)		0.9479 (0.6306, 1.4249)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7970
Odds Ratio (OR) (95% CI)		0.9219 (0.4961, 1.7129)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7969
Risk Difference (RD) (95% CI)		-0.0183 (-0.1577, 0.1211)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7968
Subjects with non-severe events (Maximum Grade 1/2)	26 (28.57)	24 (27.59)
Relative Risk (RR) (95% CI)		0.9655 (0.6031, 1.5457)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8838
Odds Ratio (OR) (95% CI)		0.9524 (0.4951, 1.8319)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8838

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Risk Difference (RD) (95% CI)		-0.0099 (-0.1419, 0.1222)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8837
Subjects with severe events (Maximum Grade 3/4/5)	6 (6.59)	5 (5.75)
Relative Risk (RR) (95% CI)		0.8716 (0.2760, 2.7524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8149
Odds Ratio (OR) (95% CI)		0.8638 (0.2538, 2.9405)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8148
Risk Difference (RD) (95% CI)		-0.0085 (-0.0791, 0.0622)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8144
Subjects with serious events	13 (14.29)	8 (9.20)
Relative Risk (RR) (95% CI)		0.6437 (0.2806, 1.4765)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2983

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Odds Ratio (OR) (95% CI)		0.6076 (0.2386, 1.5471)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2961
Risk Difference (RD) (95% CI)		-0.0509 (-0.1450, 0.0432)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2891

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	38 (34.23)	28 (25.69)
Relative Risk (RR) (95% CI)		0.7504 (0.4978, 1.1311)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1702
Odds Ratio (OR) (95% CI)		0.6641 (0.3712, 1.1880)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1678
Risk Difference (RD) (95% CI)		-0.0855 (-0.2060, 0.0350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1645
Subjects with non-severe events (Maximum Grade 1/2)	35 (31.53)	28 (25.69)
Relative Risk (RR) (95% CI)		0.8147 (0.5348, 1.2409)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3398
Odds Ratio (OR) (95% CI)		0.7506 (0.4172, 1.3505)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3384

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Risk Difference (RD) (95% CI)		-0.0584 (-0.1776, 0.0607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3365
Subjects with severe events (Maximum Grade 3/4/5)	3 (2.70)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0270 (-0.0572, 0.0031)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0791
Subjects with serious events	10 (9.01)	3 (2.75)
Relative Risk (RR) (95% CI)		0.3055 (0.0864, 1.0801)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0657

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Odds Ratio (OR) (95% CI)		0.2858 (0.0765, 1.0686)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0627
Risk Difference (RD) (95% CI)		-0.0626 (-0.1241, -0.0011)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0461

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.4.1.1
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with at least one Pulmonary Exacerbation	60 (29.70)	50 (25.51)
Relative Risk (RR) (95% CI)		0.8711 (0.6366, 1.1920)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3885
Odds Ratio (OR) (95% CI)		0.8104 (0.5172, 1.2699)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.3590
Risk Difference (RD) (95% CI)		-0.0451 (-0.1305, 0.0403)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.3002
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	17 (8.42)	8 (4.08)
Relative Risk (RR) (95% CI)		0.5004 (0.2216, 1.1301)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0958
Odds Ratio (OR) (95% CI)		0.4770 (0.2002, 1.1363)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0946
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	26 (12.87)	10 (5.10)
Relative Risk (RR) (95% CI)		0.4038 (0.2005, 0.8133)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0111
Odds Ratio (OR) (95% CI)		0.3671 (0.1713, 0.7866)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0100
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

Subgroup	P-value for Interaction
Subjects with at least one Pulmonary Exacerbation	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %) [1]	0.9656
Age at screening (<18 years vs. ≥18 years) [2]	0.2895
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.0767
Sex (Male vs. Female) [1]	0.4917
Region (North America vs. Rest of the World) [1]	0.9768
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %) [1]	0.2984
Age at screening (<18 years vs. ≥18 years) [2]	0.9038
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	N/C
Sex (Male vs. Female) [1]	0.4802*
Region (North America vs. Rest of the World) [1]	0.9365

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, age at screening (<18 vs ≥18 years) treatment*subgroup, with adjustment for continuous baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, and treatment*subgroup, with adjustment for baseline ppFEV$_1$and baseline sweat chloride as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 1.4.1.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

Subgroup	P-value for Interaction
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.3051
Age at screening (<18 years vs. ≥18 years) [2]	0.7347
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	N/C
Sex (Male vs. Female) [1]	0.6099
Region (North America vs. Rest of the World) [1]	0.9984

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, age at screening (<18 vs ≥18 years) treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, and treatment*subgroup, with adjustment for baseline $ppFEV_1$and baseline sweat chloride as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Percent predicted FEV1 at Baseline <70%

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Subjects with at least one Pulmonary Exacerbation	41 (35.96)	32 (31.68)
Relative Risk (RR) (95% CI)		0.8796 (0.6028, 1.2836)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.5059
Odds Ratio (OR) (95% CI)		0.8161 (0.4585, 1.4528)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4899
Risk Difference (RD) (95% CI)		-0.0584 (-0.1897, 0.0728)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.3828
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	11 (9.65)	3 (2.97)
Relative Risk (RR) (95% CI)		0.3239 (0.0928, 1.1305)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0771
Odds Ratio (OR) (95% CI)		0.3019 (0.0811, 1.1243)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0742
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Percent predicted FEV1 at Baseline <70%

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	19 (16.67)	5 (4.95)
Relative Risk (RR) (95% CI)		0.3021 (0.1166, 0.7825)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0137
Odds Ratio (OR) (95% CI)		0.2637 (0.0940, 0.7396)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0113
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Percent predicted FEV1 at Baseline ≥70%

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Subjects with at least one Pulmonary Exacerbation	19 (21.84)	18 (19.57)
Relative Risk (RR) (95% CI)		0.8747 (0.4943, 1.5479)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6457
Odds Ratio (OR) (95% CI)		0.8382 (0.4041, 1.7385)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6354
Risk Difference (RD) (95% CI)		-0.0335 (-0.1518, 0.0849)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.5794
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	6 (6.90)	5 (5.43)
Relative Risk (RR) (95% CI)		0.7344 (0.2111, 2.5552)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6275*
Odds Ratio (OR) (95% CI)		0.7190 (0.2065, 2.5040)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6044
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Percent predicted FEV1 at Baseline ≥70%

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	7 (8.05)	5 (5.43)
Relative Risk (RR) (95% CI)		0.6429 (0.1981, 2.0861)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4620*
Odds Ratio (OR) (95% CI)		0.6196 (0.1852, 2.0725)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4371
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with at least one Pulmonary Exacerbation	6 (19.35)	2 (7.69)
Relative Risk (RR) (95% CI)		0.3989 (0.0868, 1.8342)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2378
Odds Ratio (OR) (95% CI)		0.3507 (0.0626, 1.9639)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2332
Risk Difference (RD) (95% CI)		-0.1208 (-0.3136, 0.0720)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.2195
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	2 (6.45)	1 (3.85)
Relative Risk (RR) (95% CI)		0.3728 (0.0293, 4.7470)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4472*
Odds Ratio (OR) (95% CI)		0.3601 (0.0217, 5.9849)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4763
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	2 (6.45)	1 (3.85)
Relative Risk (RR) (95% CI)		0.3728 (0.0293, 4.7470)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4472*
Odds Ratio (OR) (95% CI)		0.3601 (0.0217, 5.9849)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4763
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with at least one Pulmonary Exacerbation	54 (31.58)	48 (28.24)
Relative Risk (RR) (95% CI)		0.9069 (0.6569, 1.2520)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.5526
Odds Ratio (OR) (95% CI)		0.8666 (0.5417, 1.3862)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.5501
Risk Difference (RD) (95% CI)		-0.0300 (-0.1274, 0.0674)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.5455
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	15 (8.77)	7 (4.12)
Relative Risk (RR) (95% CI)		0.4869 (0.2038, 1.1636)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1054
Odds Ratio (OR) (95% CI)		0.4636 (0.1835, 1.1714)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.1041
Risk Difference (RD) (95% CI)		-0.0454 (-0.0967, 0.0060)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.0834

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	24 (14.04)	9 (5.29)
Relative Risk (RR) (95% CI)		0.3863 (0.1851, 0.8060)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0113
Odds Ratio (OR) (95% CI)		0.3488 (0.1565, 0.7771)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0100
Risk Difference (RD) (95% CI)		-0.0903 (-0.1545, -0.0260)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.0059

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with at least one Pulmonary Exacerbation	7 (36.84)	2 (11.76)
Relative Risk (RR) (95% CI)		0.3332 (0.0795, 1.3966)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1328*
Odds Ratio (OR) (95% CI)		0.2151 (0.0300, 1.5409)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.1261
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	2 (10.53)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	5 (26.32)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with at least one Pulmonary Exacerbation	53 (29.12)	48 (27.12)
Relative Risk (RR) (95% CI)		0.9465 (0.6838, 1.3100)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7401
Odds Ratio (OR) (95% CI)		0.9065 (0.5673, 1.4486)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6816
Risk Difference (RD) (95% CI)		-0.0234 (-0.1134, 0.0666)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.6103
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	15 (8.24)	8 (4.52)
Relative Risk (RR) (95% CI)		0.5664 (0.2471, 1.2983)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1792
Odds Ratio (OR) (95% CI)		0.5469 (0.2248, 1.3303)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.1833
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	21 (11.54)	10 (5.65)
Relative Risk (RR) (95% CI)		0.5066 (0.2469, 1.0395)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0637
Odds Ratio (OR) (95% CI)		0.4739 (0.2151, 1.0441)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0639
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Subjects with at least one Pulmonary Exacerbation	29 (24.37)	29 (25.00)
Relative Risk (RR) (95% CI)		1.0018 (0.6427, 1.5614)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.9938
Odds Ratio (OR) (95% CI)		0.9934 (0.5428, 1.8183)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.9830
Risk Difference (RD) (95% CI)		-0.0030 (-0.1126, 0.1066)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.9571
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	6 (5.04)	4 (3.45)
Relative Risk (RR) (95% CI)		0.7314 (0.2102, 2.5443)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6229*
Odds Ratio (OR) (95% CI)		0.7205 (0.1922, 2.7012)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6269
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	12 (10.08)	4 (3.45)
Relative Risk (RR) (95% CI)		0.3254 (0.1080, 0.9808)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0461
Odds Ratio (OR) (95% CI)		0.2991 (0.0924, 0.9679)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0440
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Subjects with at least one Pulmonary Exacerbation	31 (37.35)	21 (26.25)
Relative Risk (RR) (95% CI)		0.7945 (0.5097, 1.2383)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3096
Odds Ratio (OR) (95% CI)		0.6725 (0.3364, 1.3442)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2615
Risk Difference (RD) (95% CI)		-0.0831 (-0.2269, 0.0607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.2574
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	11 (13.25)	4 (5.00)
Relative Risk (RR) (95% CI)		0.3850 (0.1277, 1.1601)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0899
Odds Ratio (OR) (95% CI)		0.3512 (0.1056, 1.1679)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0878
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	14 (16.87)	6 (7.50)
Relative Risk (RR) (95% CI)		0.4782 (0.1941, 1.1779)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1087
Odds Ratio (OR) (95% CI)		0.4202 (0.1505, 1.1729)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0978
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Subjects with at least one Pulmonary Exacerbation	25 (27.47)	21 (24.14)
Relative Risk (RR) (95% CI)		0.8921 (0.5422, 1.4679)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6532
Odds Ratio (OR) (95% CI)		0.8252 (0.4155, 1.6389)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.5832
Risk Difference (RD) (95% CI)		-0.0424 (-0.1698, 0.0851)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.5148
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	11 (12.09)	5 (5.75)
Relative Risk (RR) (95% CI)		0.4995 (0.1824, 1.3682)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1770
Odds Ratio (OR) (95% CI)		0.4667 (0.1538, 1.4158)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.1783
Risk Difference (RD) (95% CI)		-0.0605 (-0.1408, 0.0199)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.1402

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	13 (14.29)	5 (5.75)
Relative Risk (RR) (95% CI)		0.4209 (0.1575, 1.1249)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0845
Odds Ratio (OR) (95% CI)		0.3812 (0.1288, 1.1277)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0814
Risk Difference (RD) (95% CI)		-0.0827 (-0.1679, 0.0025)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.0573

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Subjects with at least one Pulmonary Exacerbation	35 (31.53)	29 (26.61)
Relative Risk (RR) (95% CI)		0.8694 (0.5804, 1.3022)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4971
Odds Ratio (OR) (95% CI)		0.8118 (0.4469, 1.4745)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4935
Risk Difference (RD) (95% CI)		-0.0523 (-0.1685, 0.0638)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.3772
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	6 (5.41)	3 (2.75)
Relative Risk (RR) (95% CI)		0.5184 (0.1336, 2.0123)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3424
Odds Ratio (OR) (95% CI)		0.5015 (0.1213, 2.0722)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.3404
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

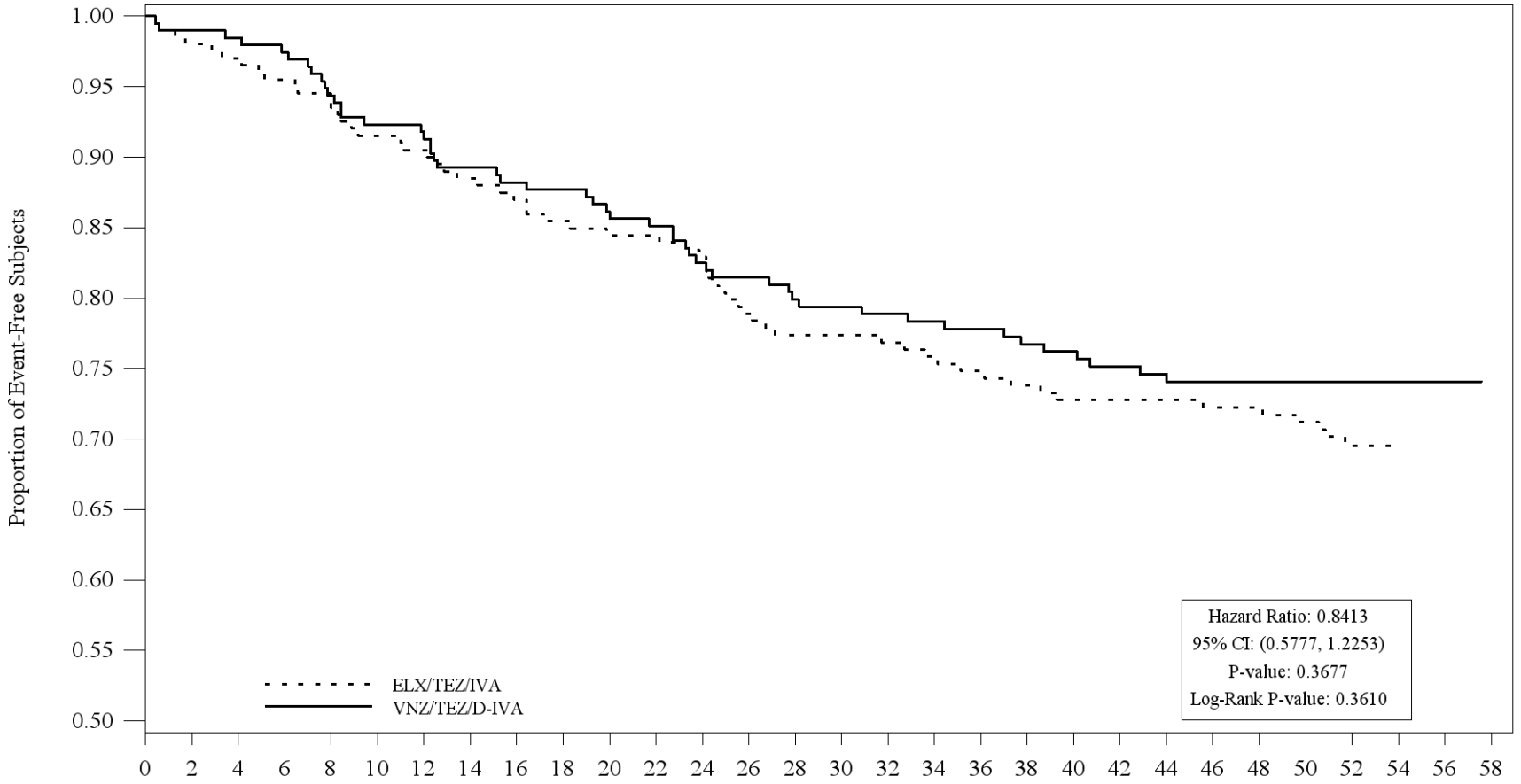
Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	13 (11.71)	5 (4.59)
Relative Risk (RR) (95% CI)		0.4011 (0.1491, 1.0786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0703
Odds Ratio (OR) (95% CI)		0.3664 (0.1248, 1.0757)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0677
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Figure 1.2.1.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52
Full Analysis Set

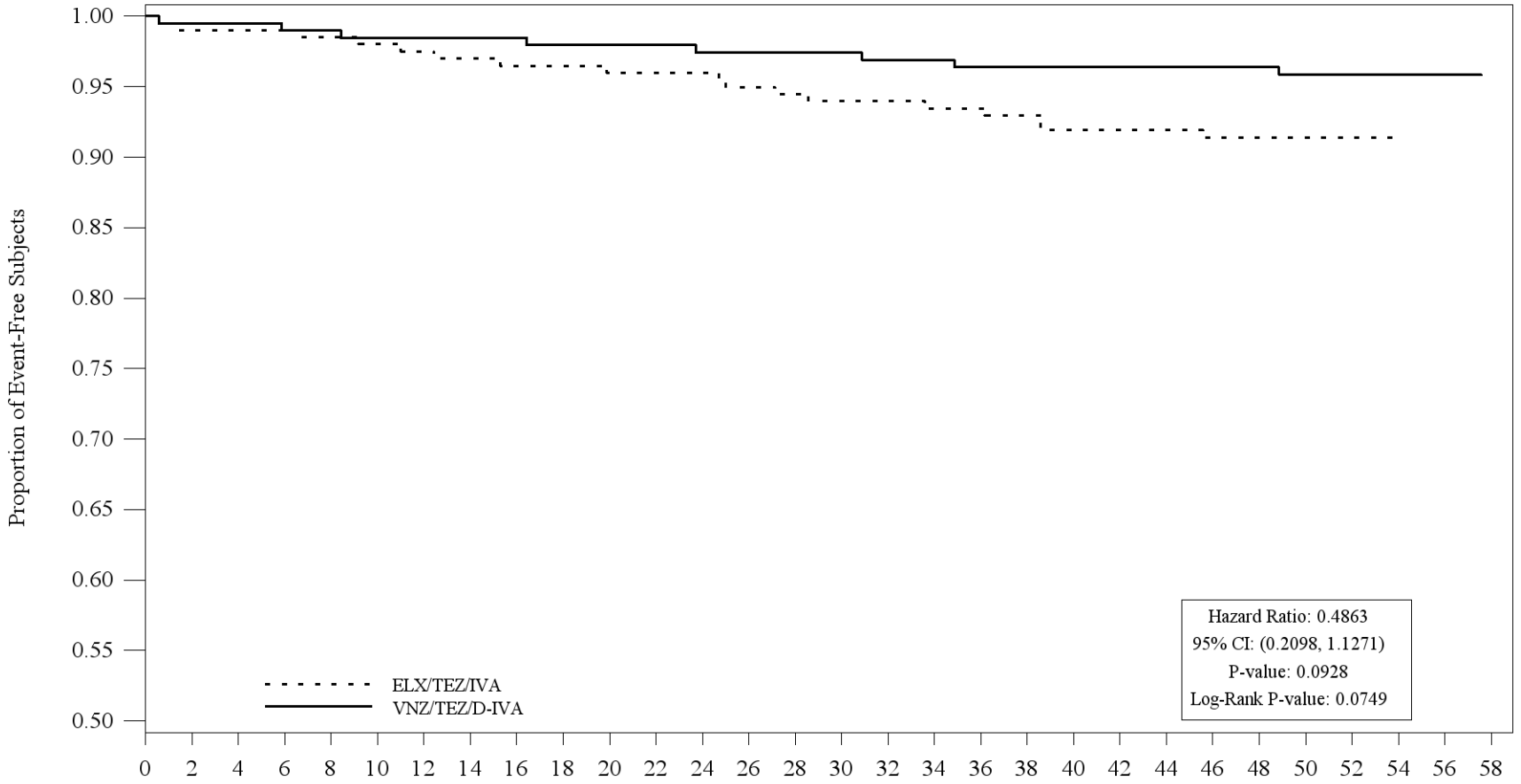


Number of patients at risk

ELX/TEZ/IVA	202	179	164	146	139
VNZ/TEZ/D-IVA	196	179	159	147	139

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 1.2.1.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

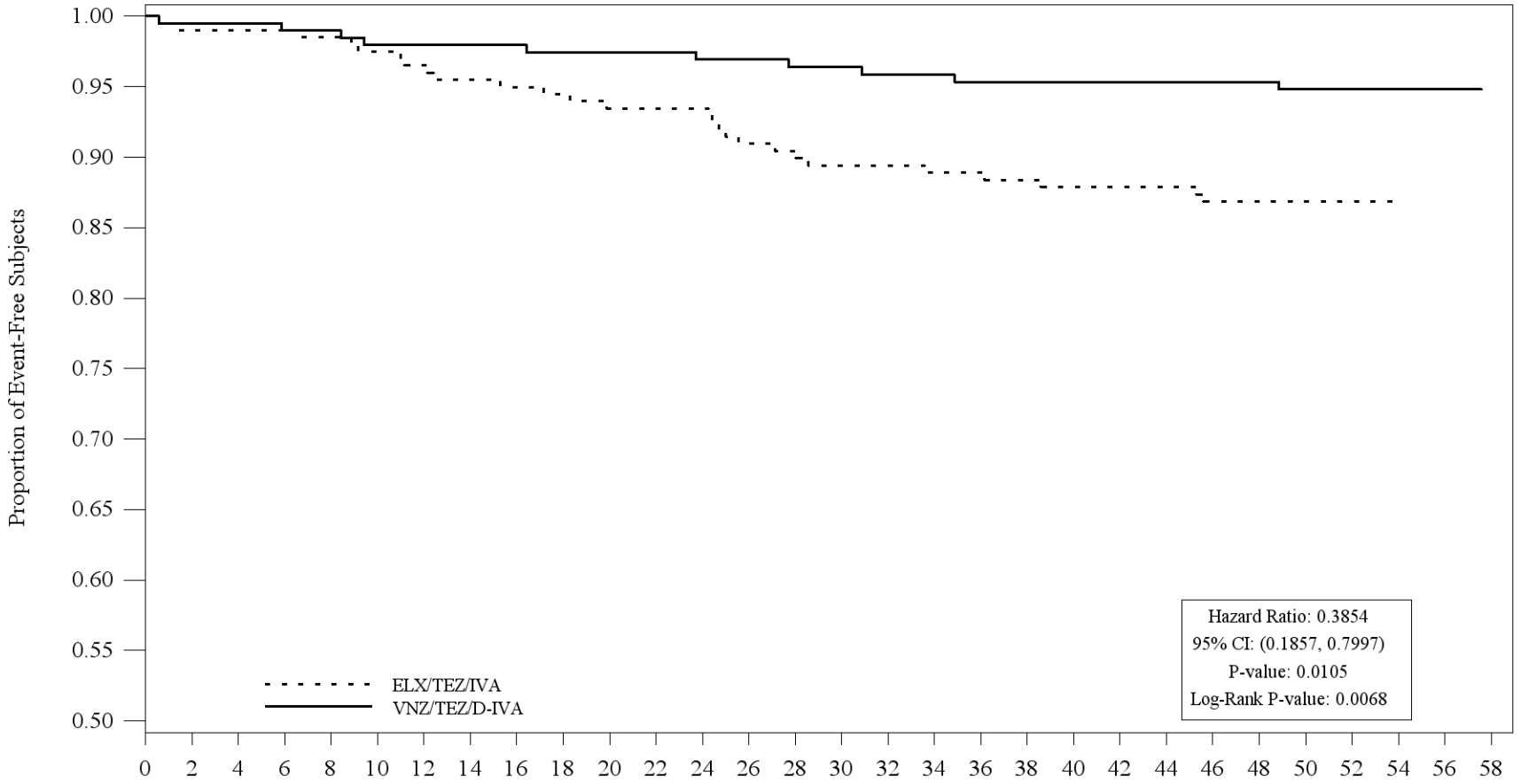


Number of patients at risk

ELX/TEZ/IVA	202	193	190	182	175
VNZ/TEZ/D-IVA	196	192	188	182	181

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 1.2.1.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set



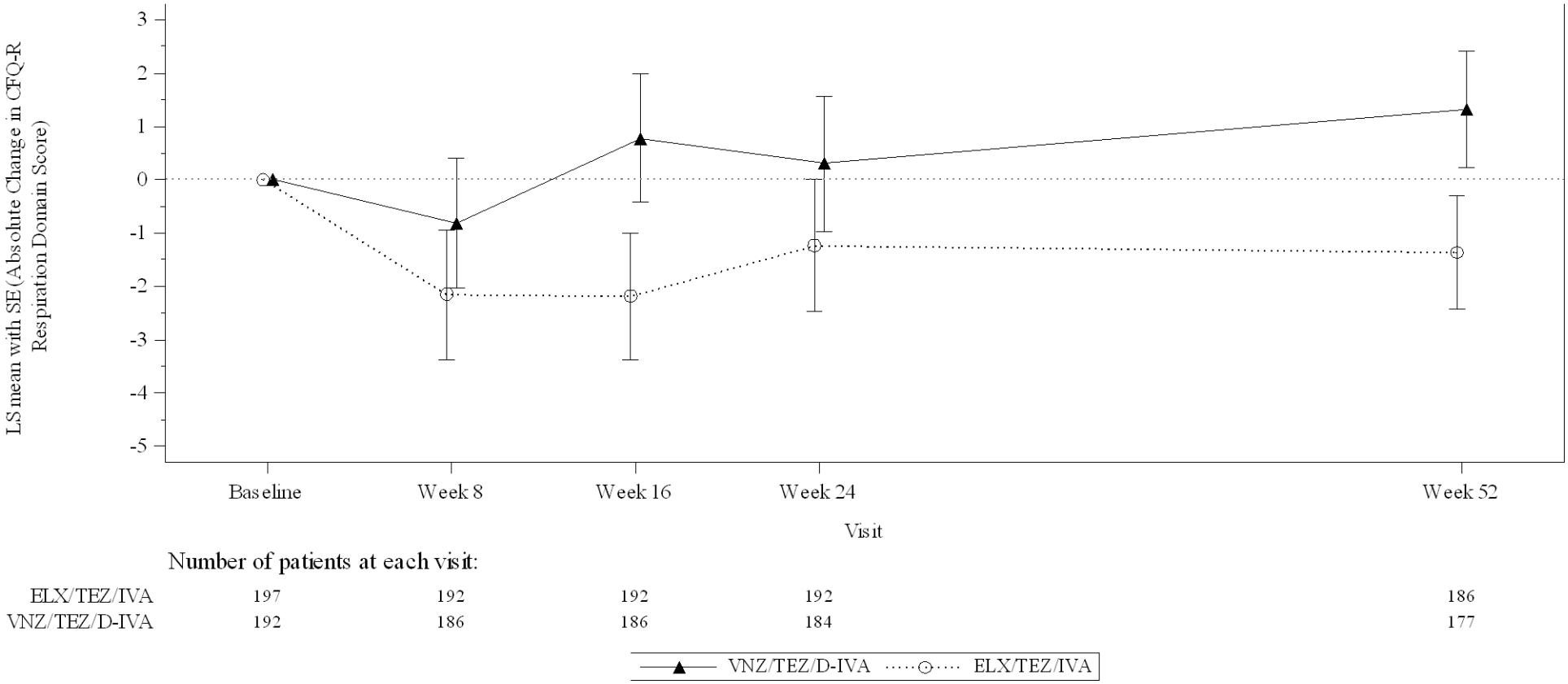
Number of patients at risk

ELX/TEZ/IVA	202	191	185	173	166
VNZ/TEZ/D-IVA	196	191	187	180	179

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration

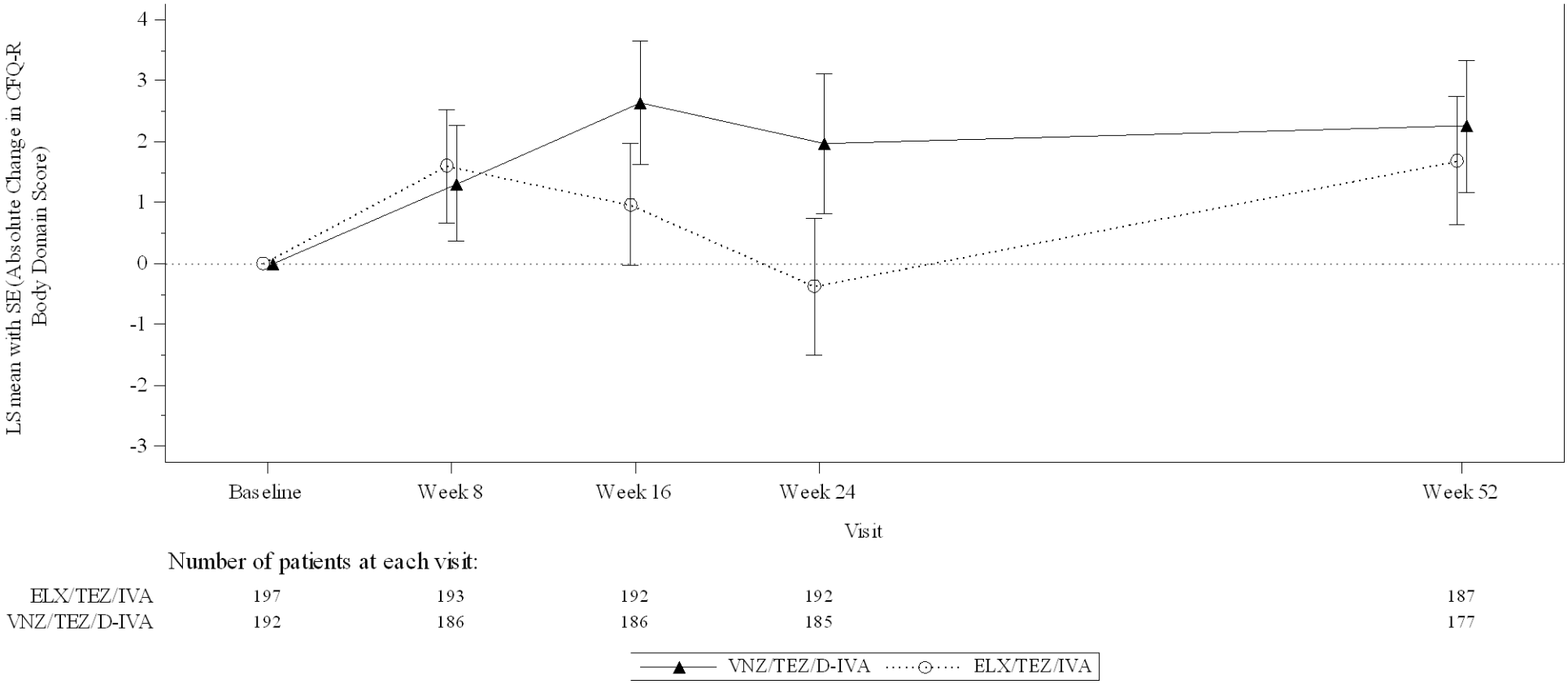


- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

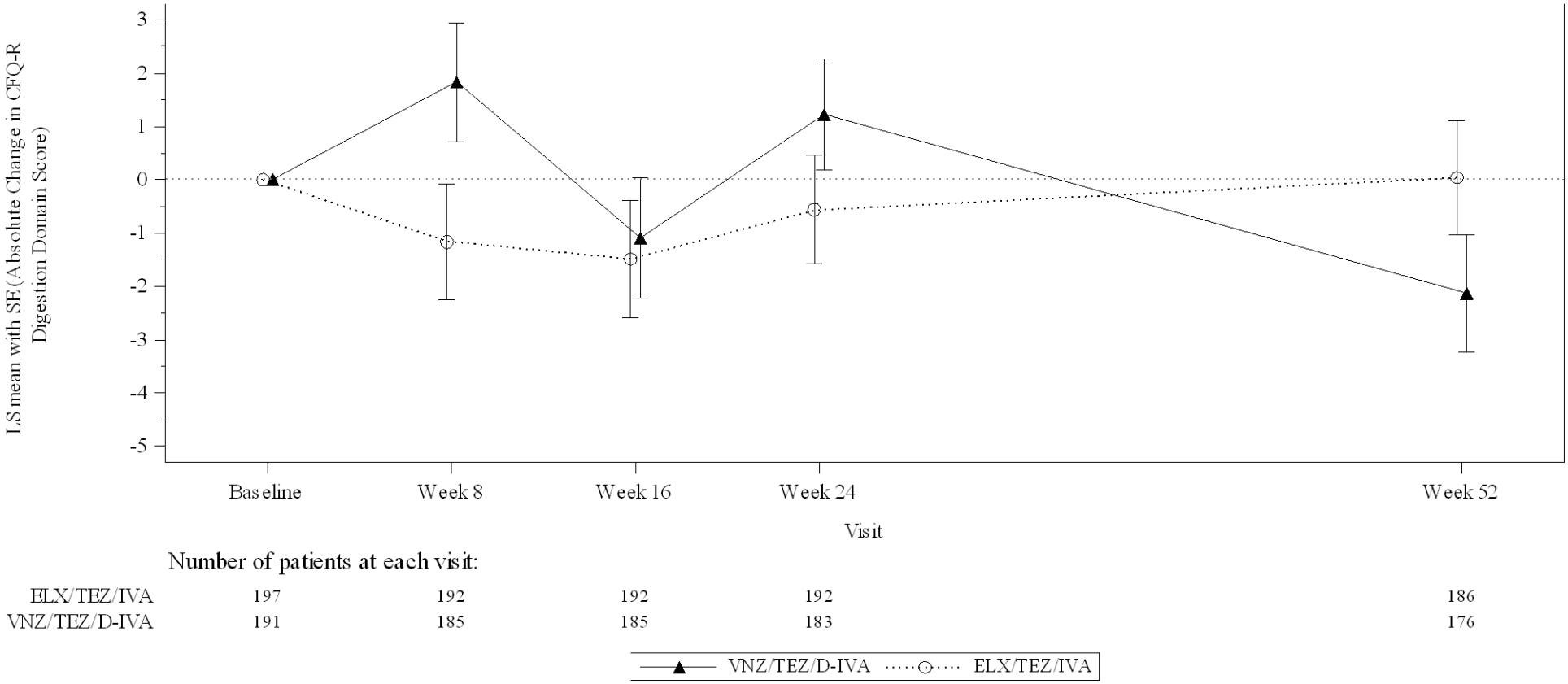


- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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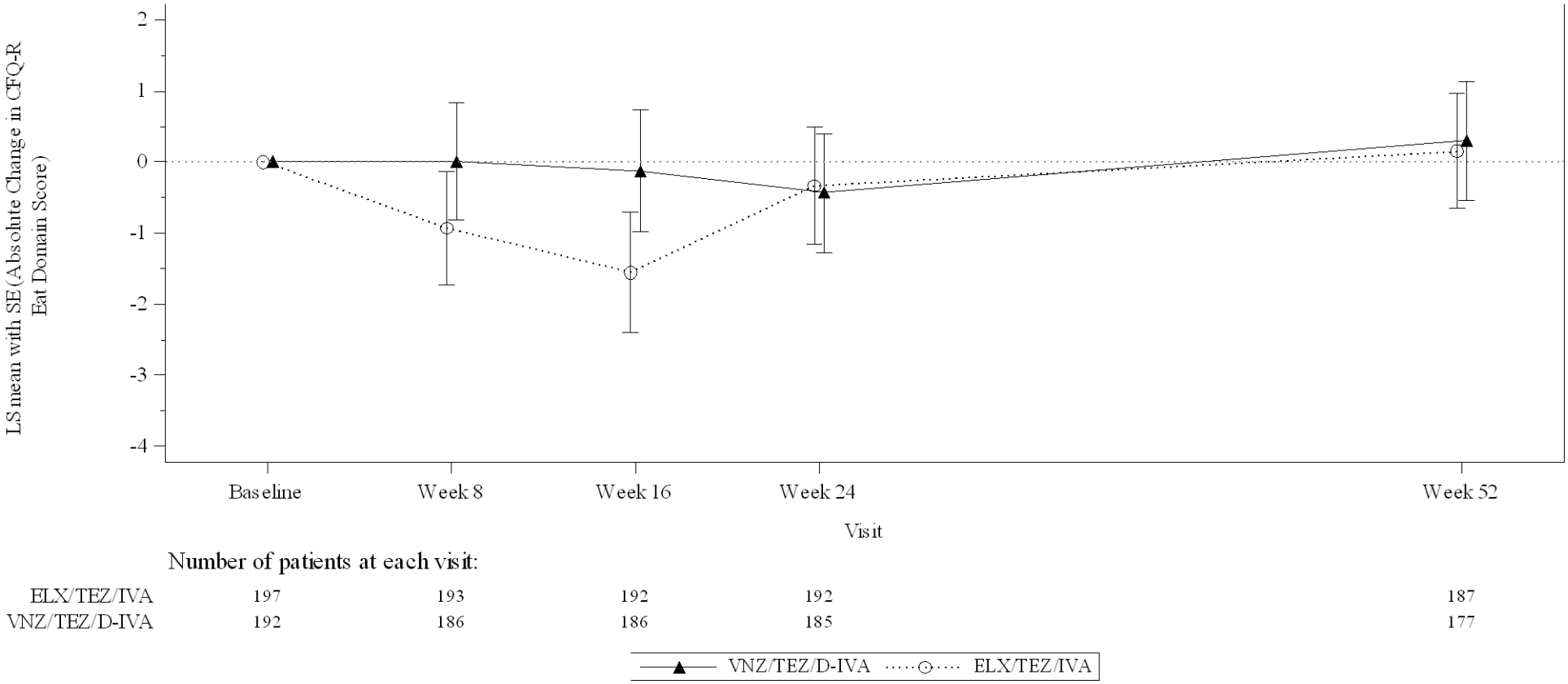
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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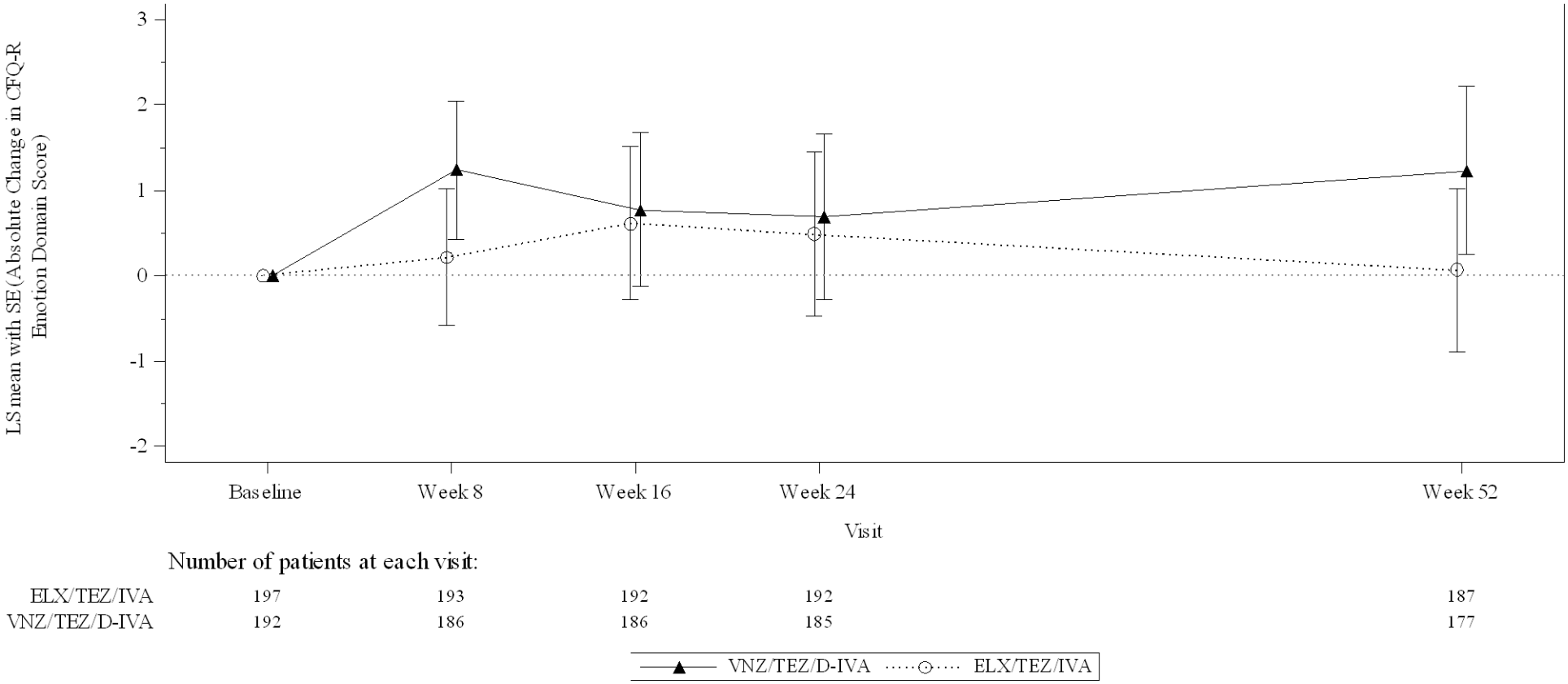
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion



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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions

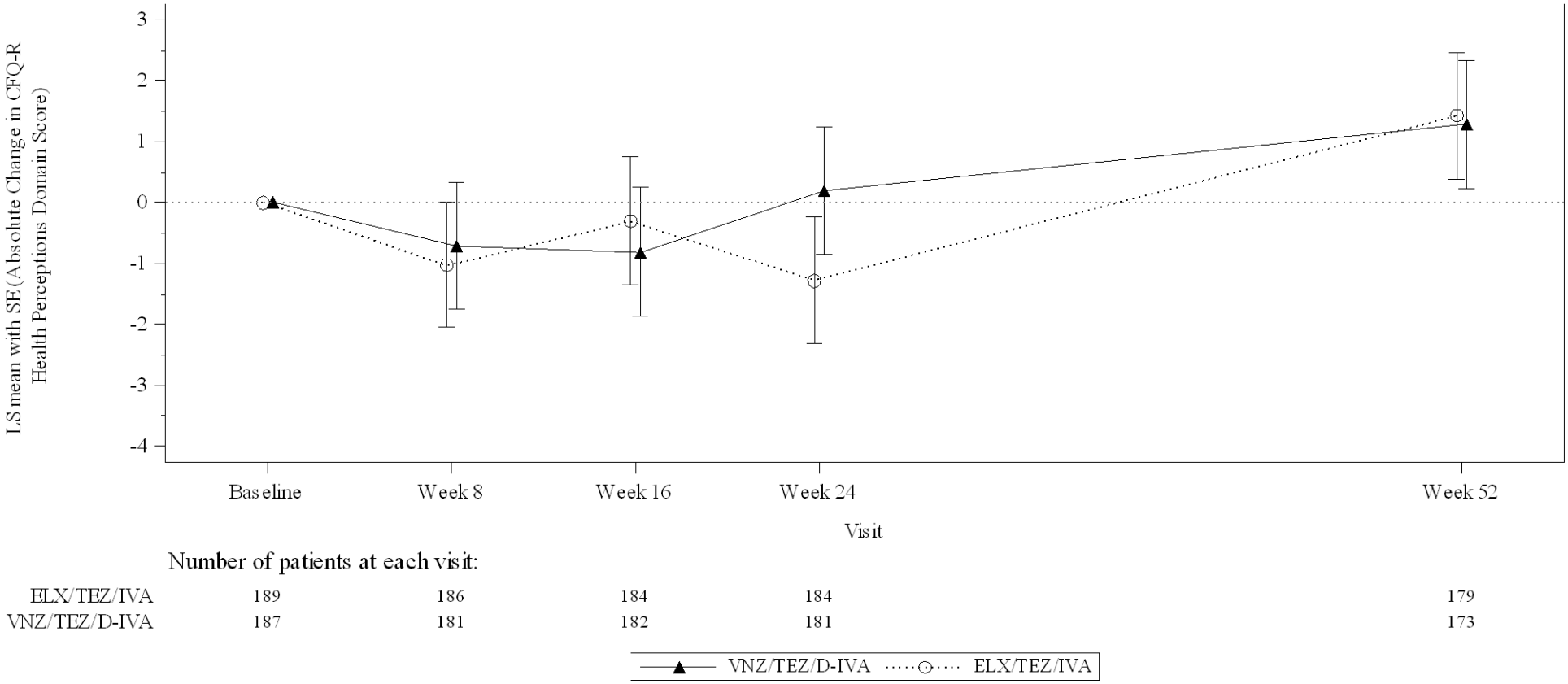

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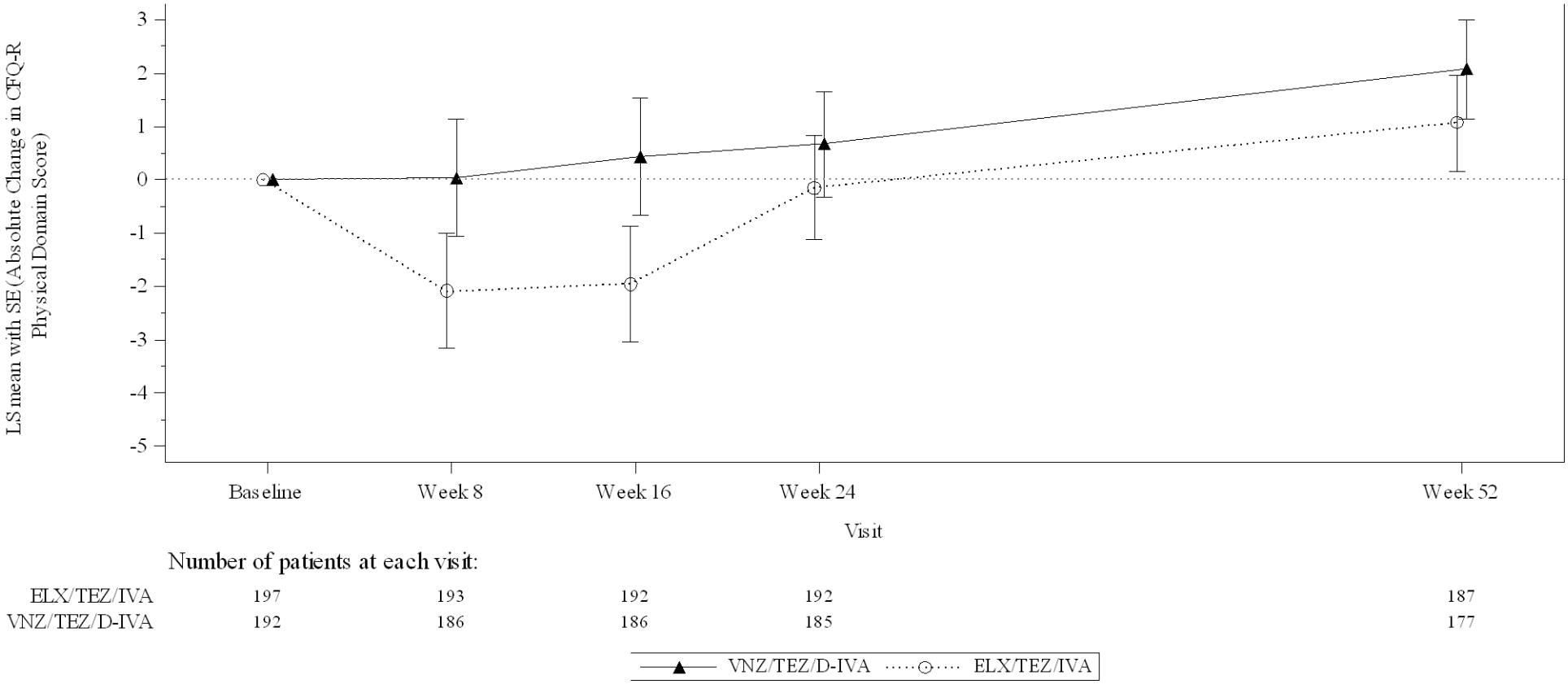
Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical



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- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role

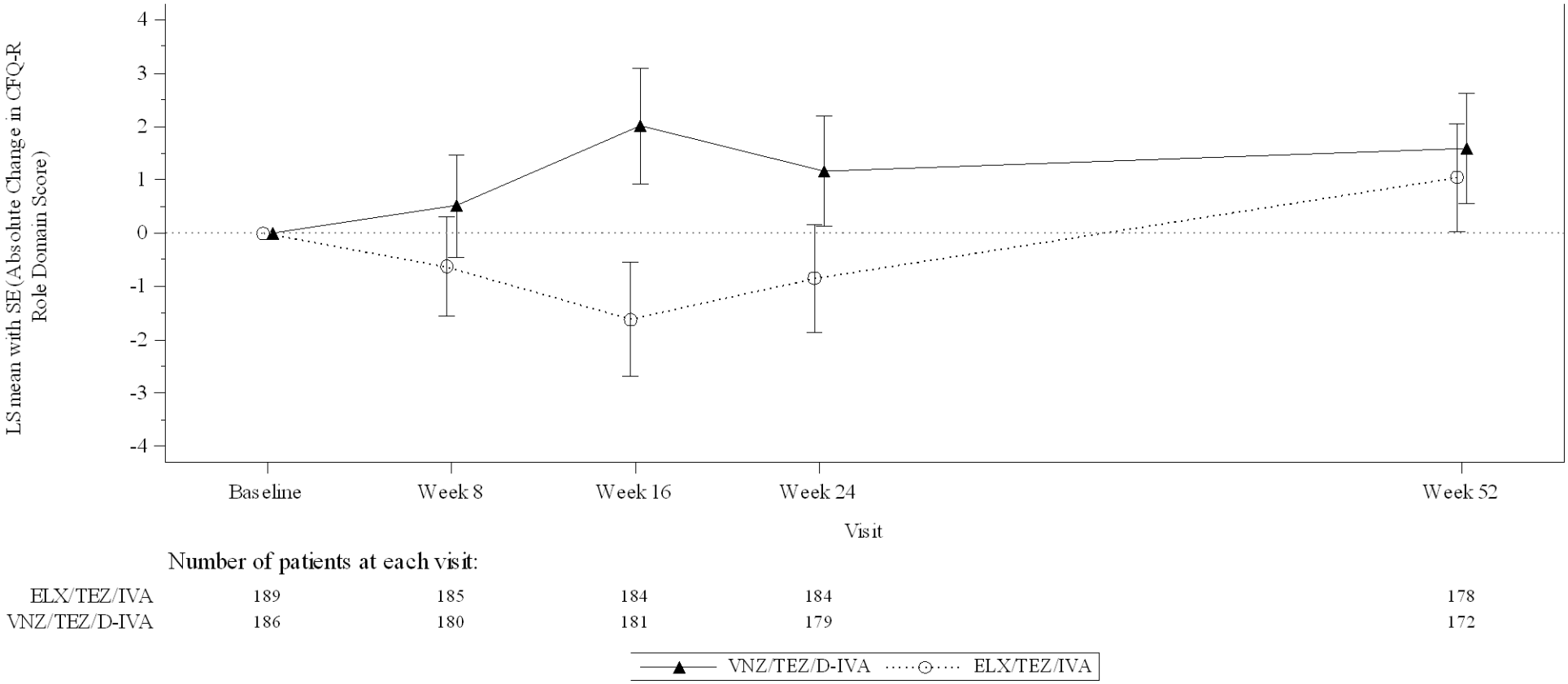

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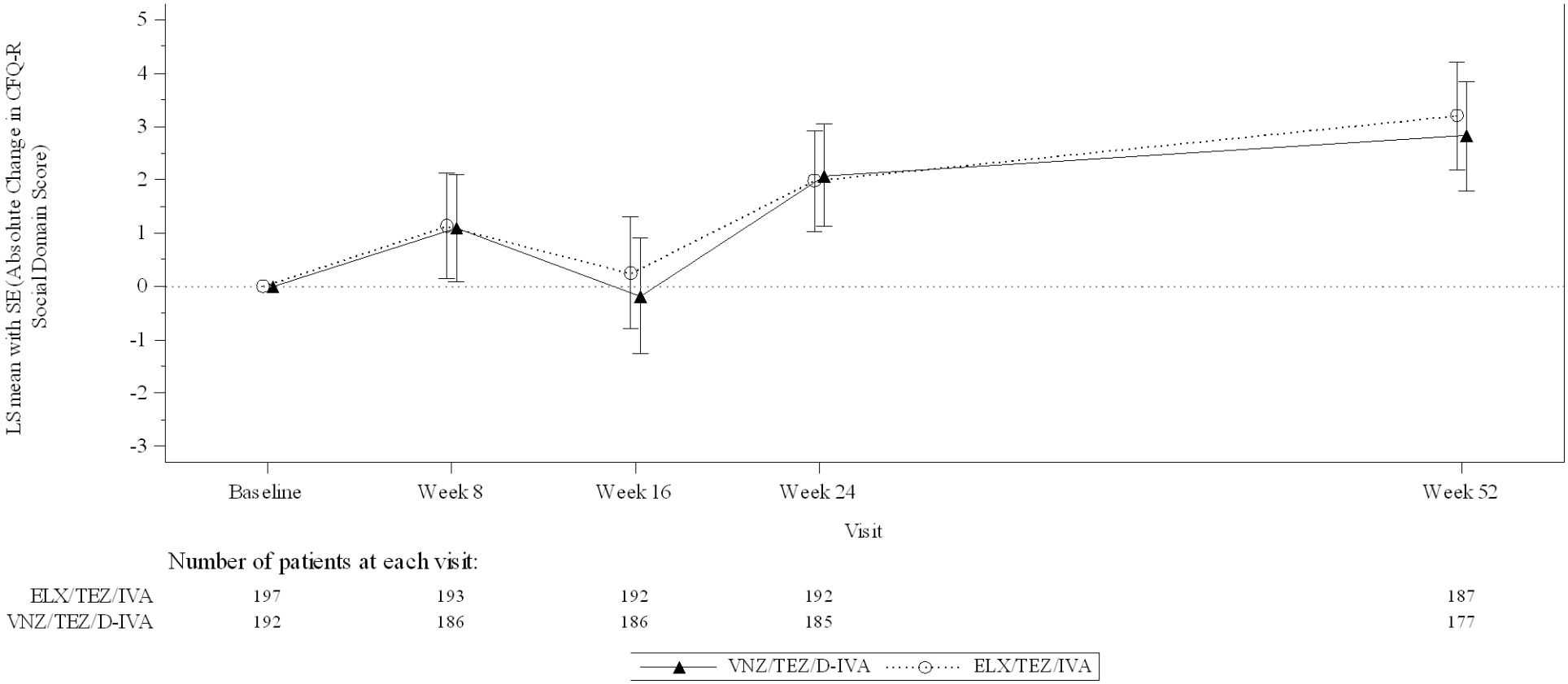
Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social



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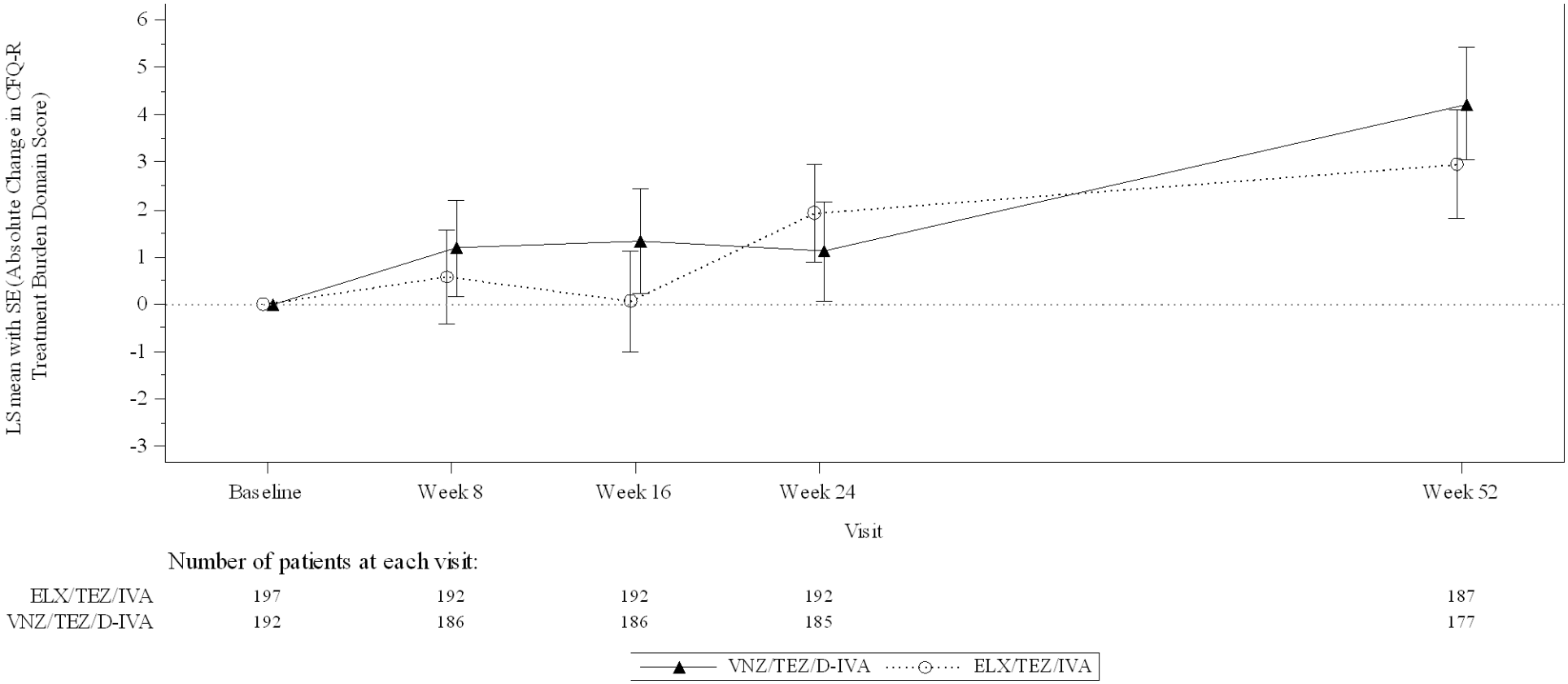
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden



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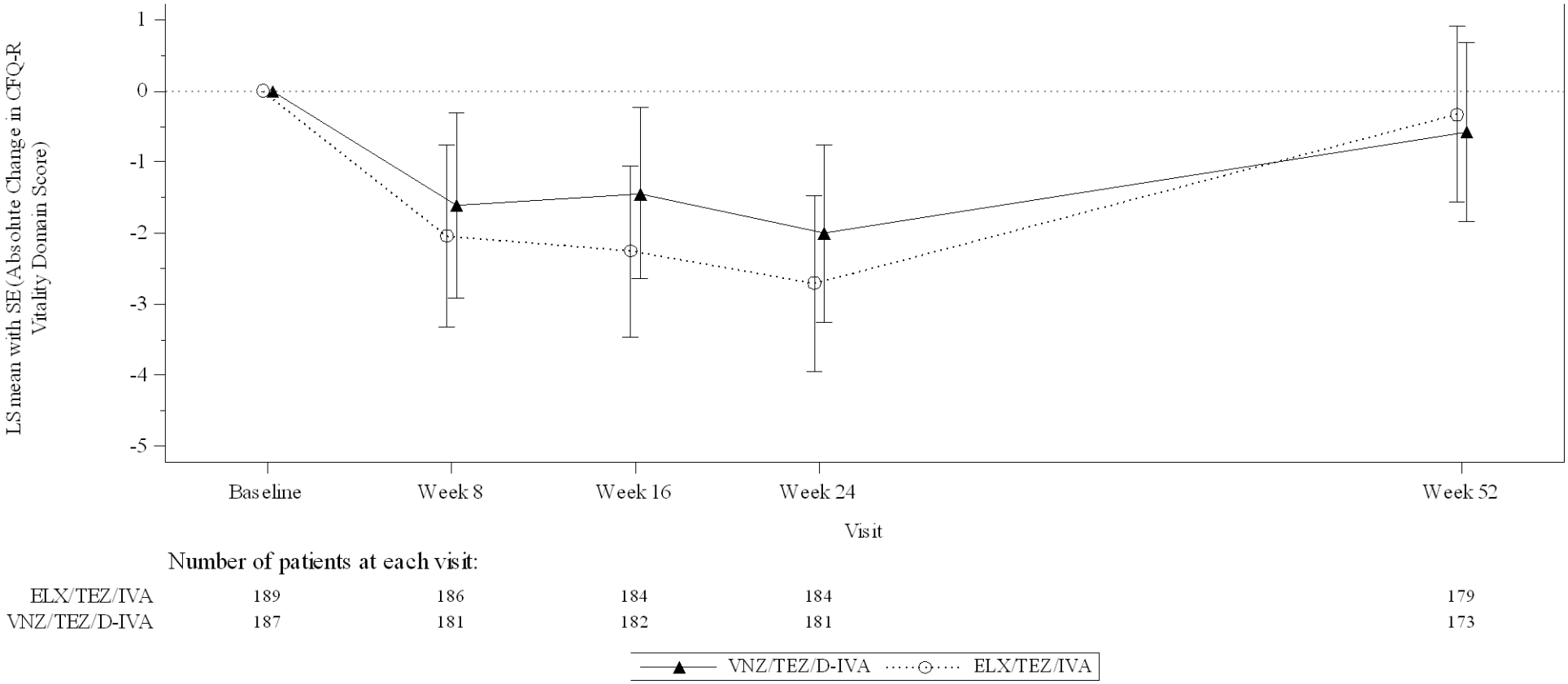
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality



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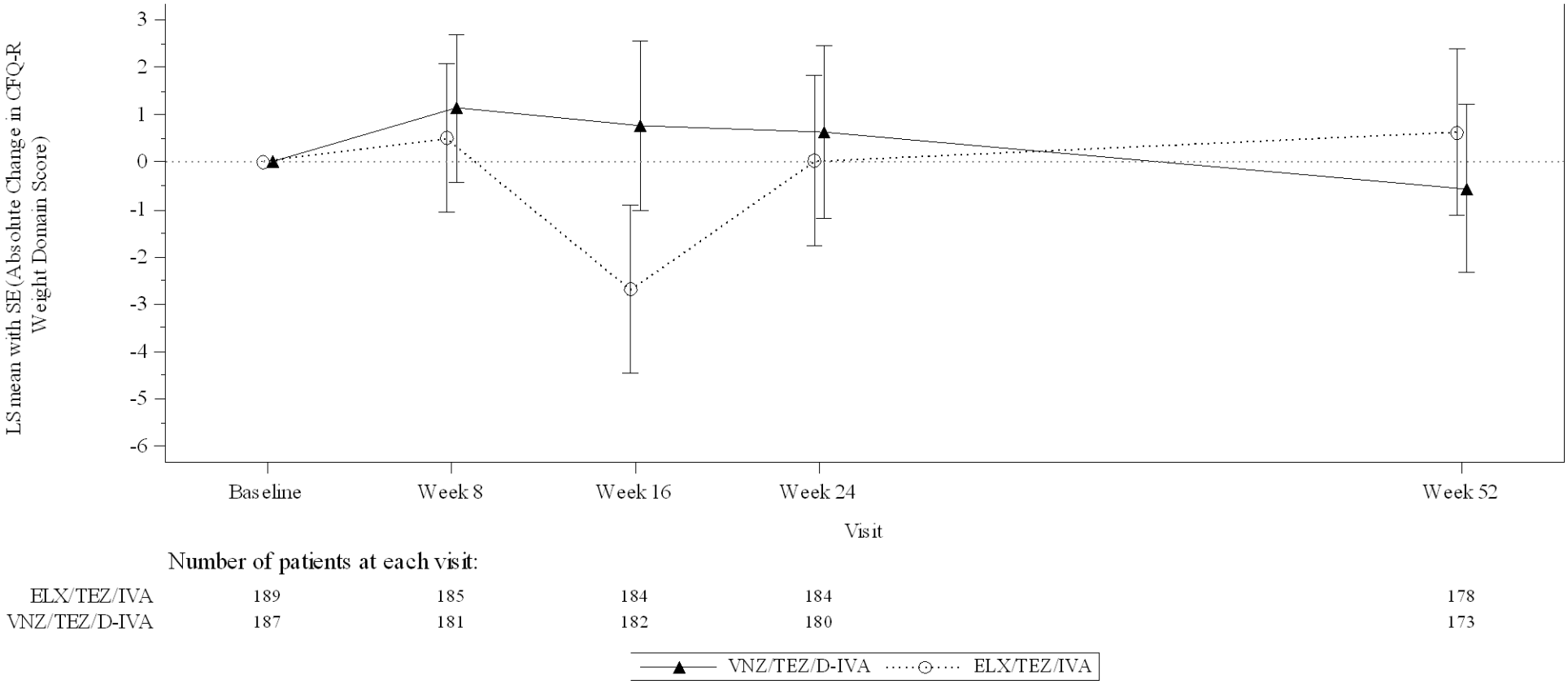
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight



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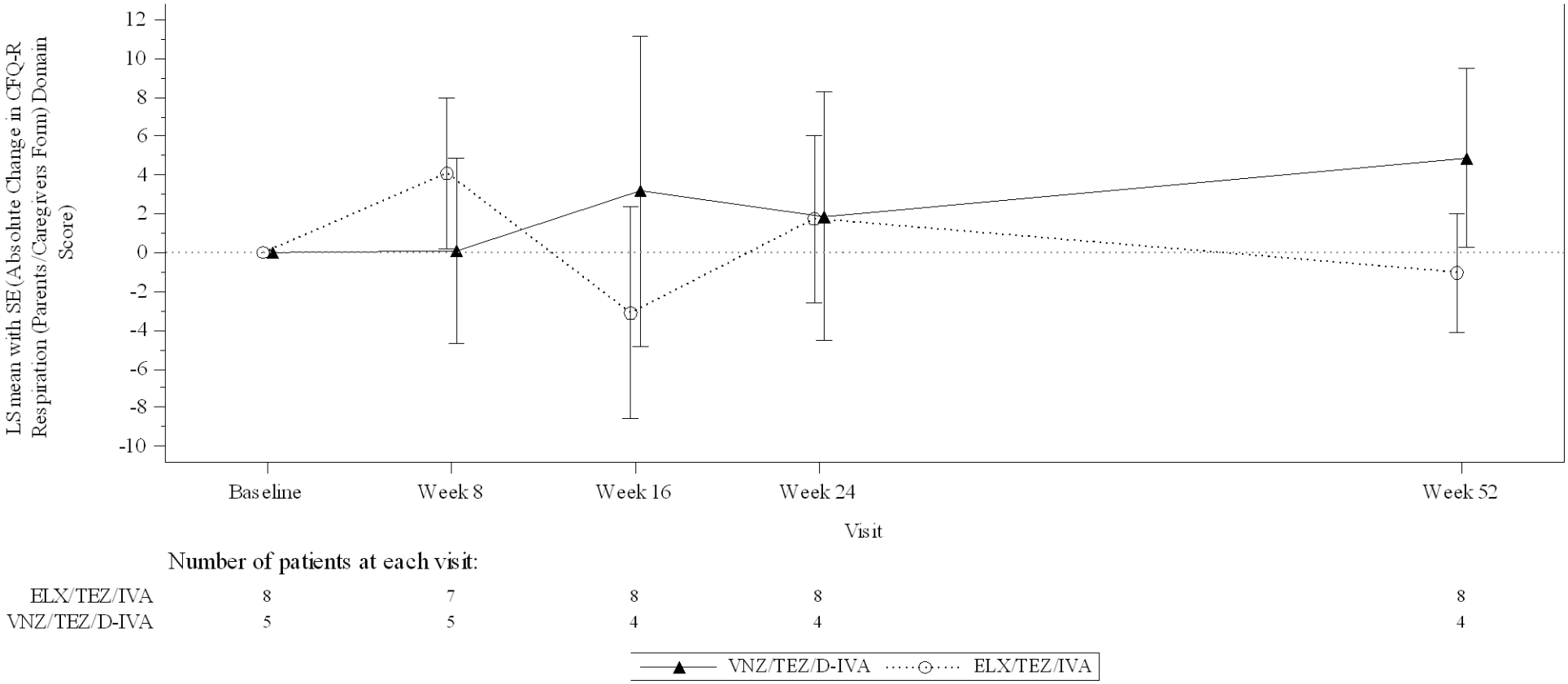
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)



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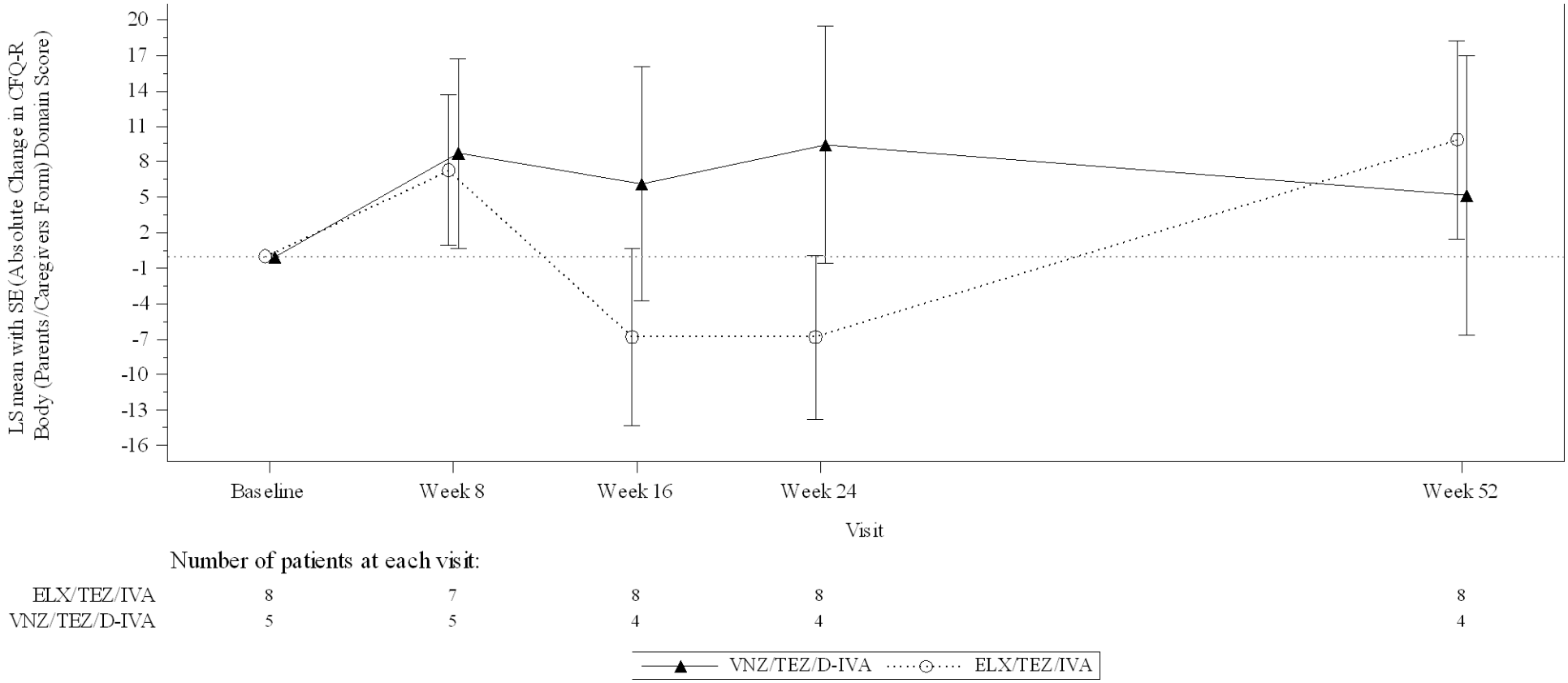
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)



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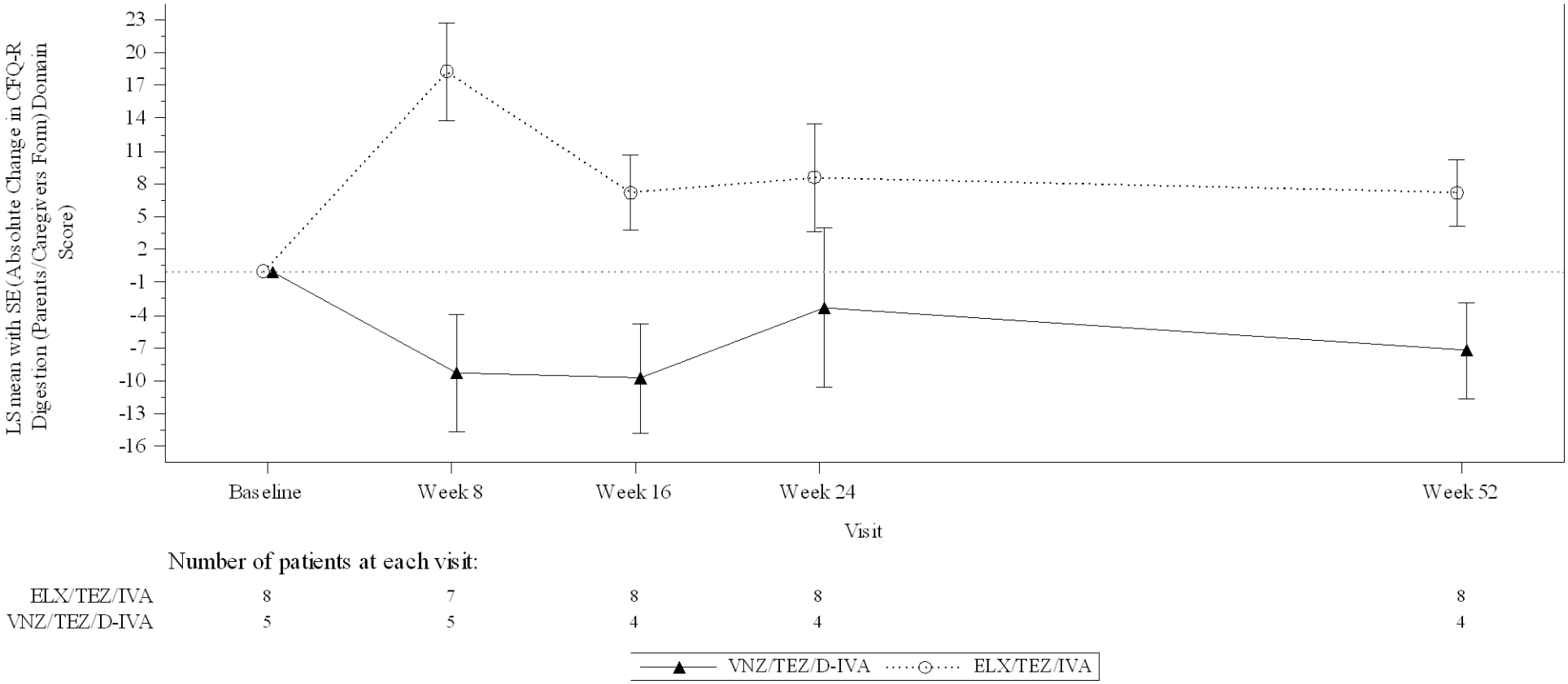
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)



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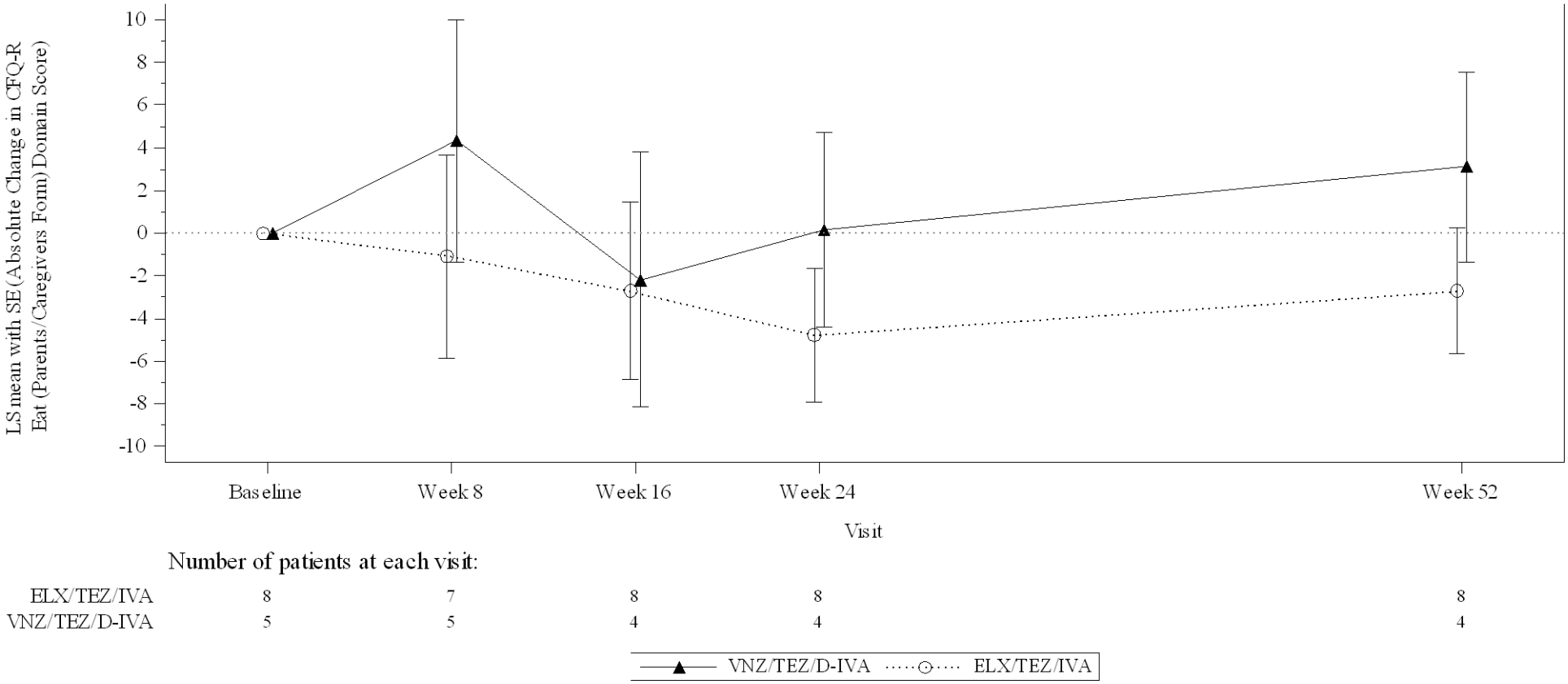
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)



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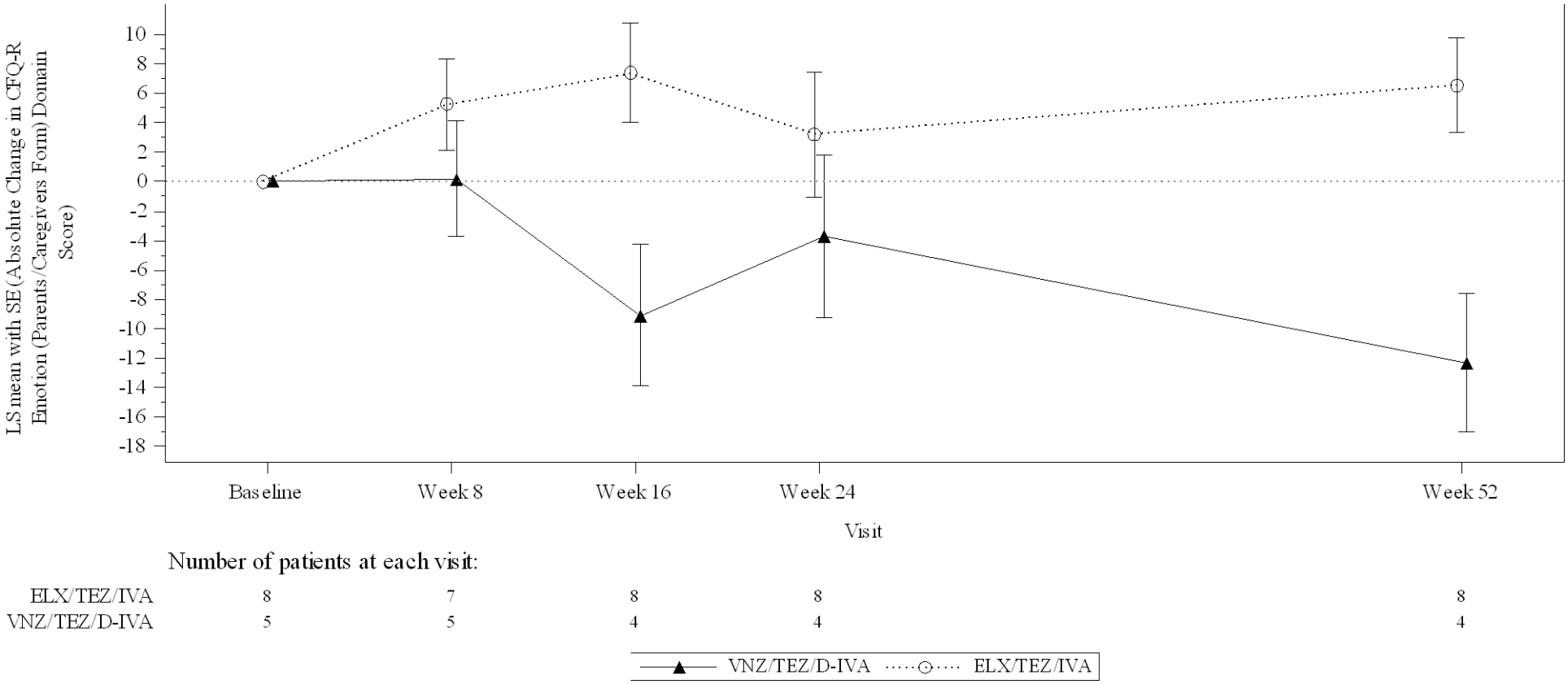
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)



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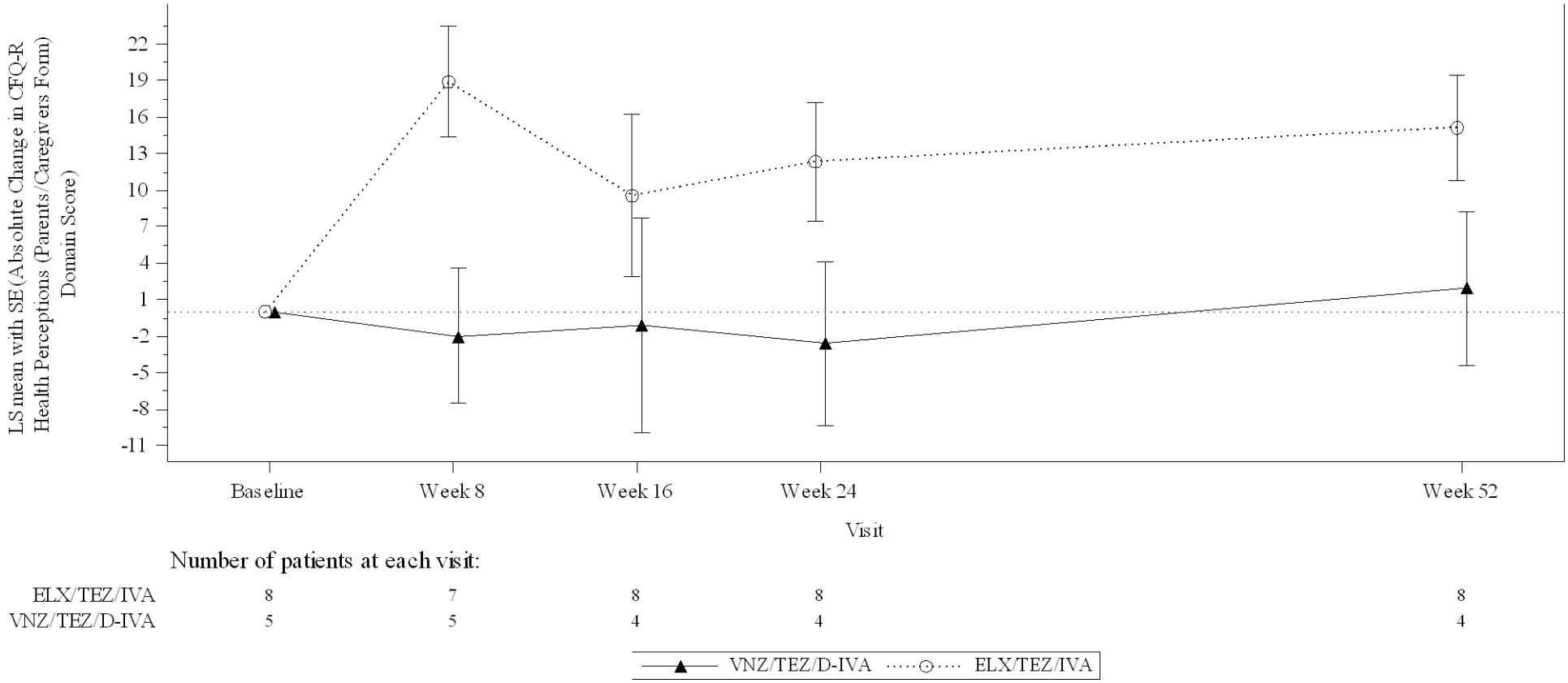
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)



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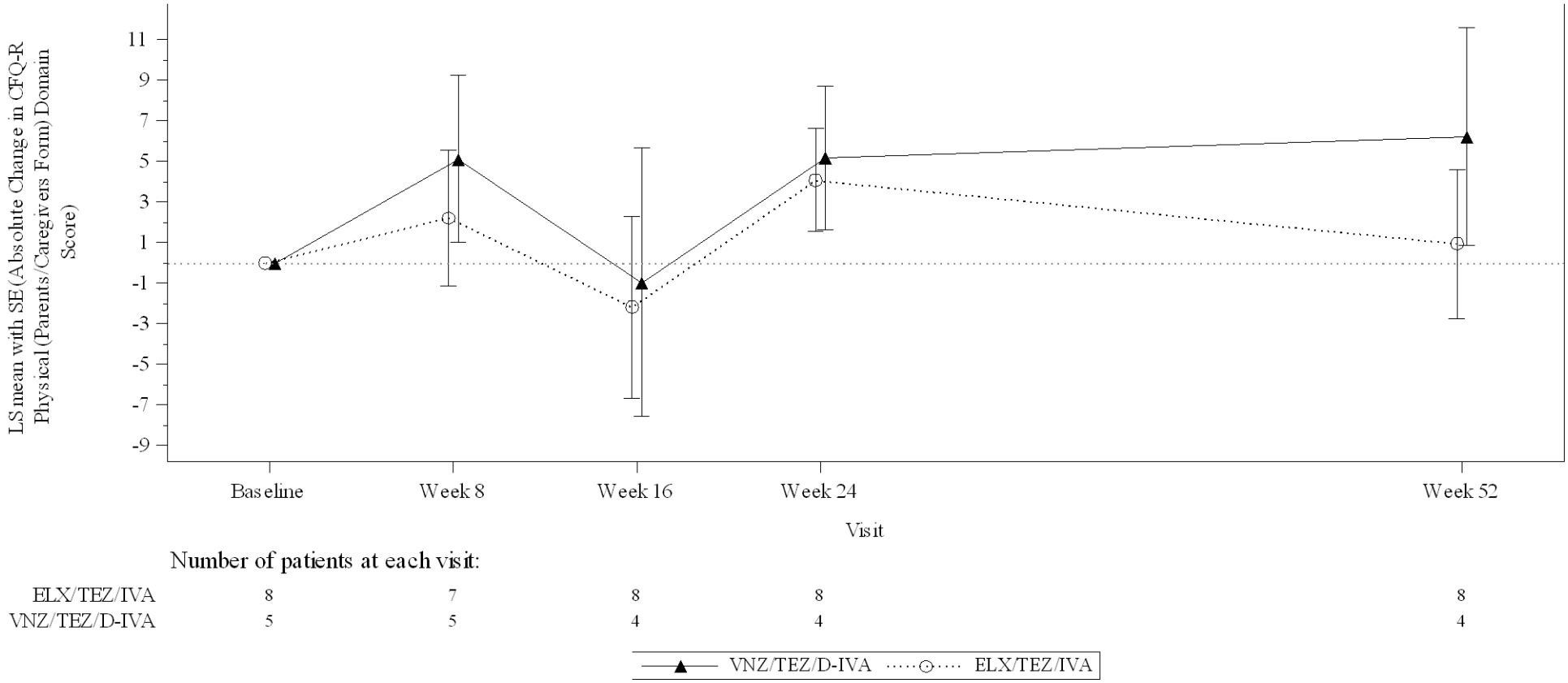
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)



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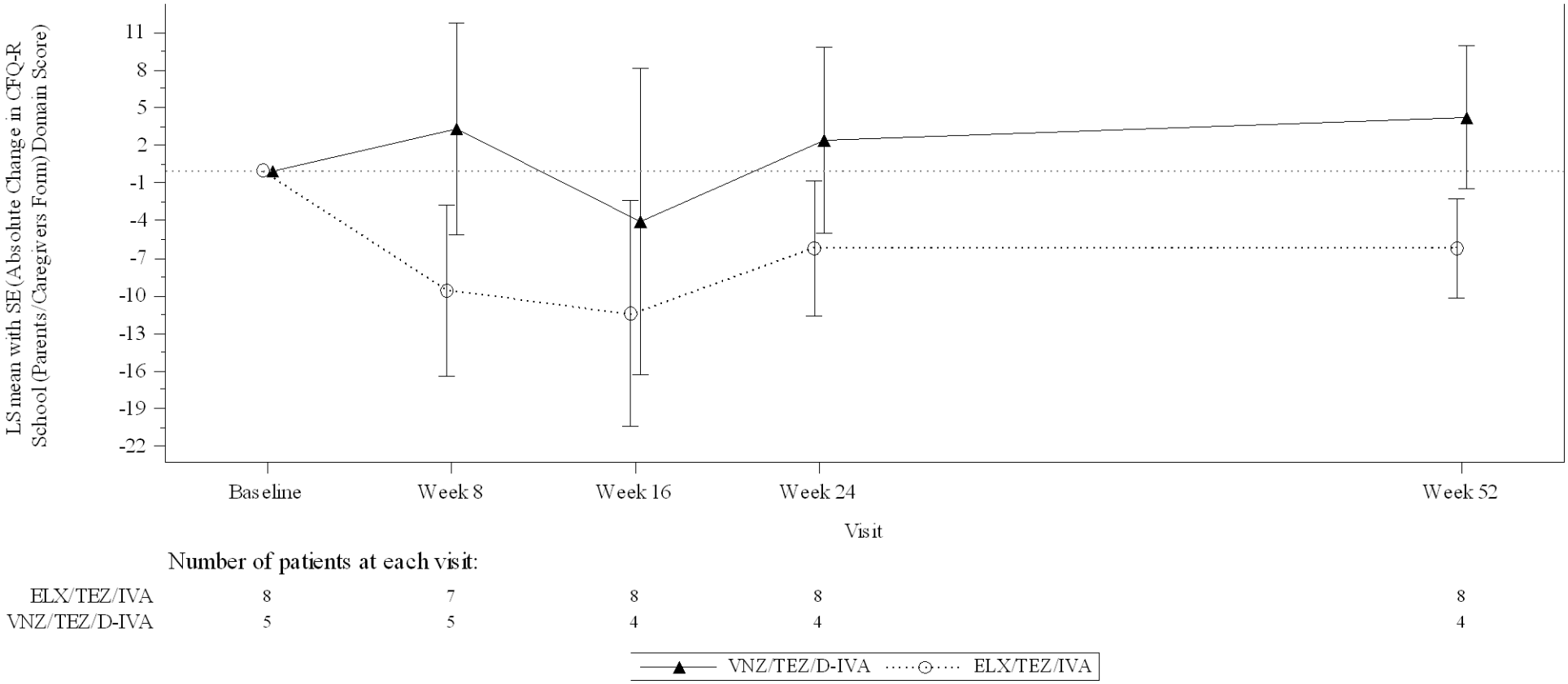
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)



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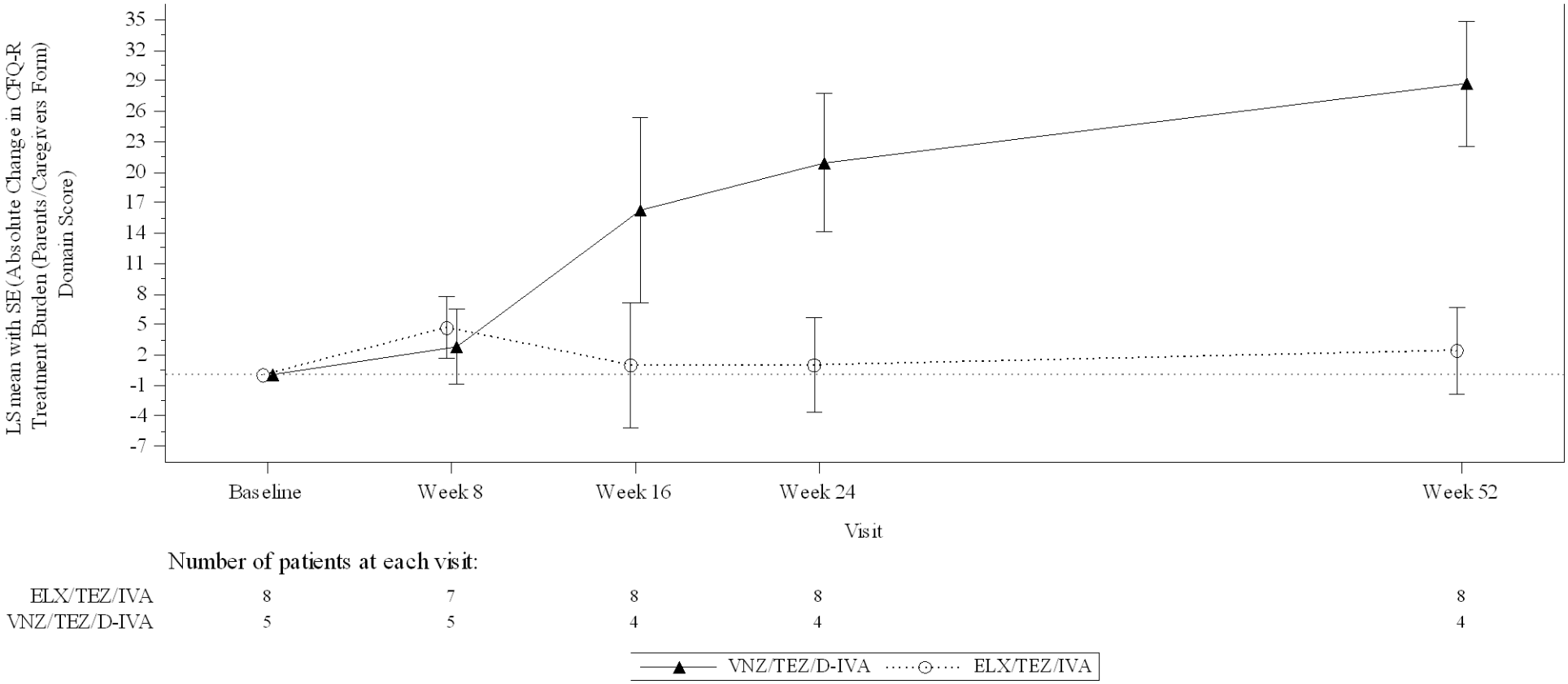
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)



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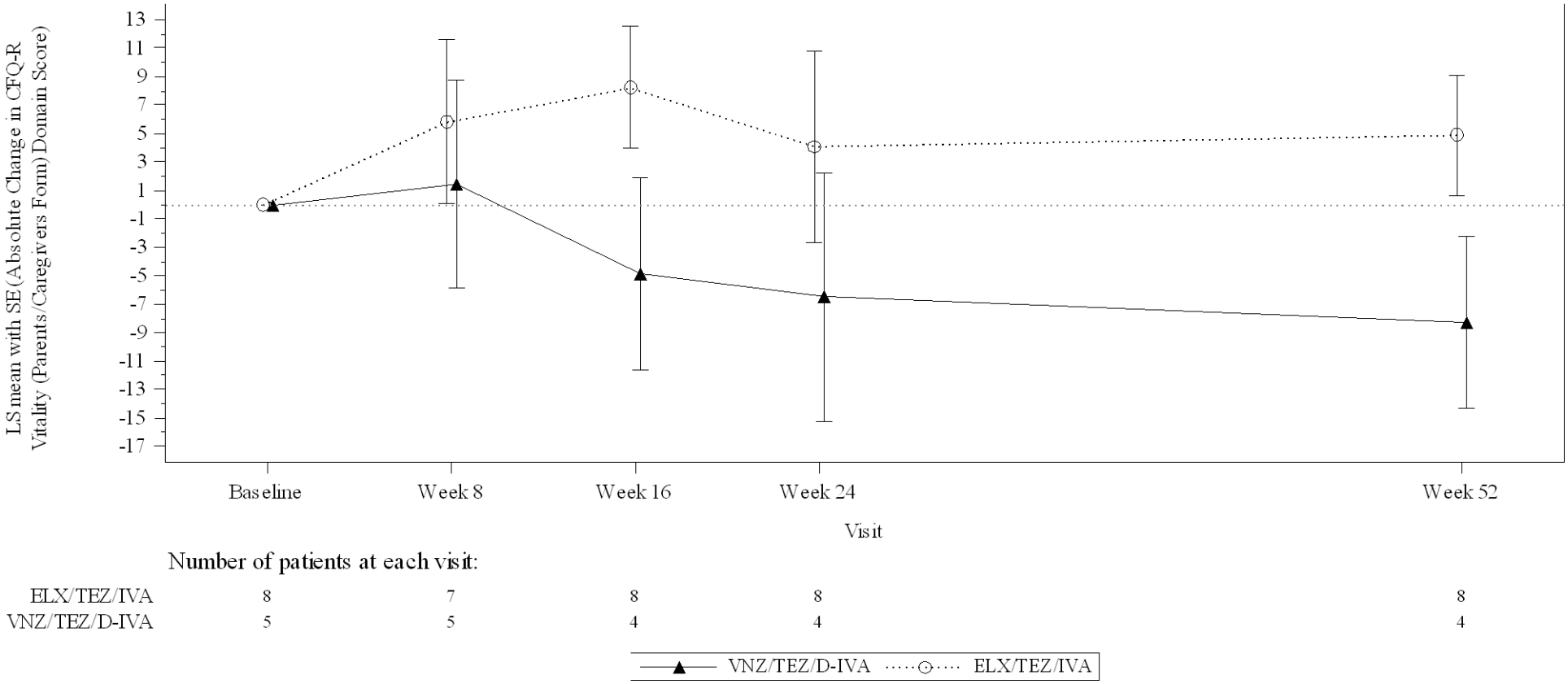
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)



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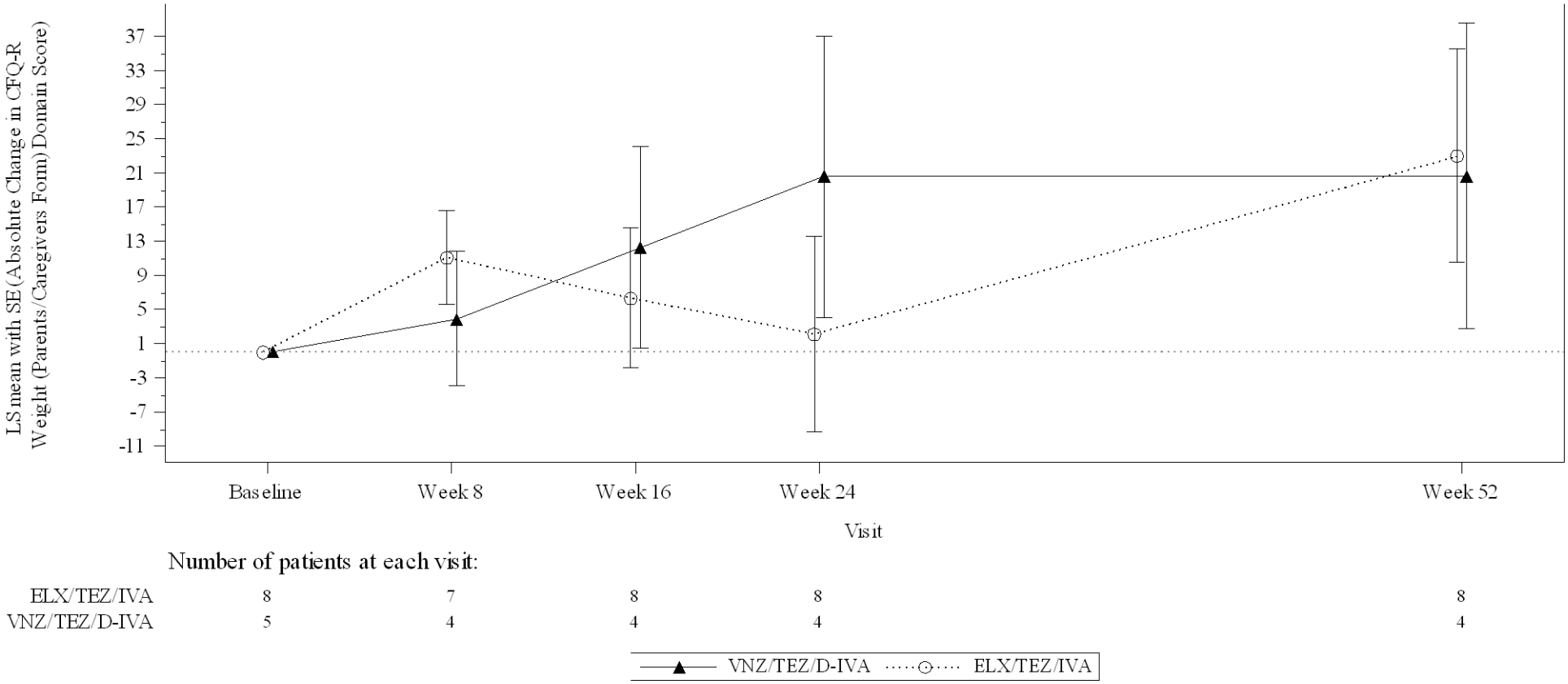
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)



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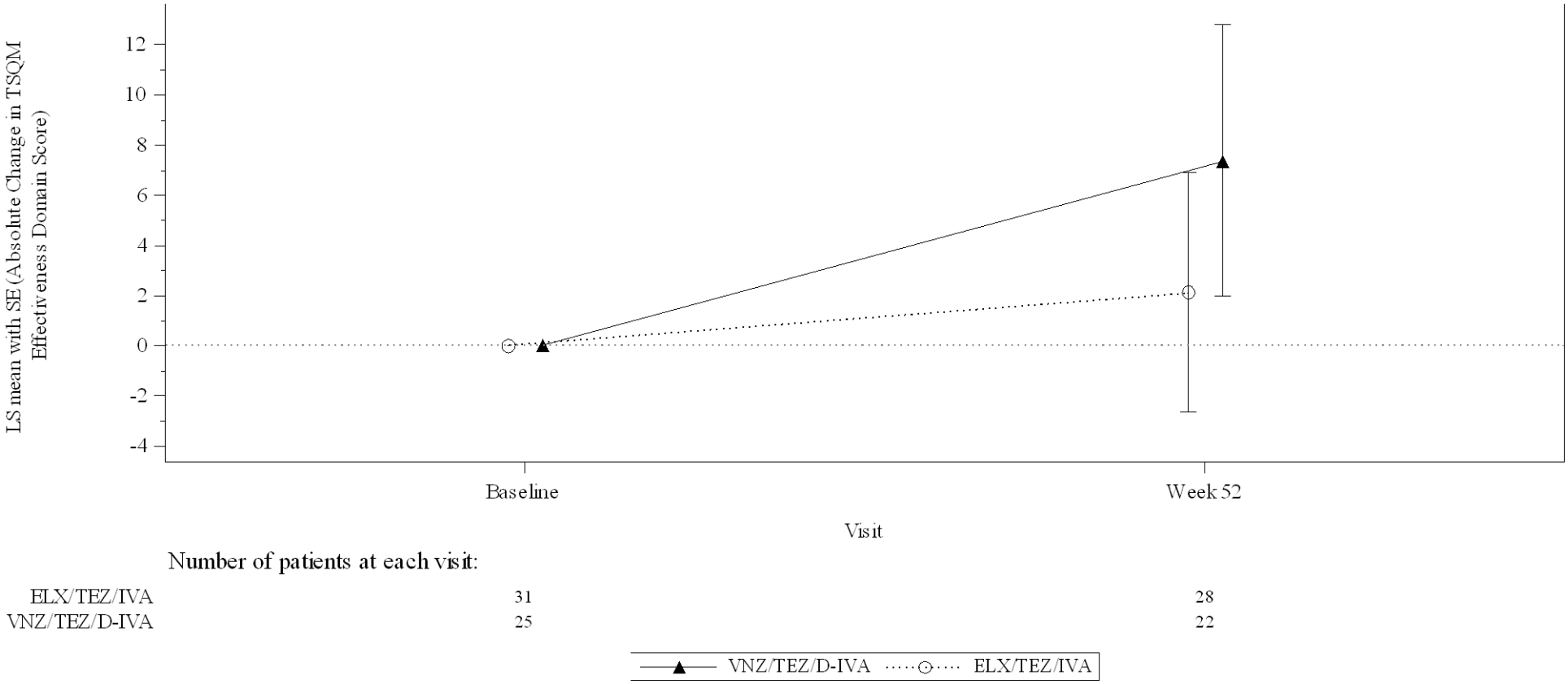
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness



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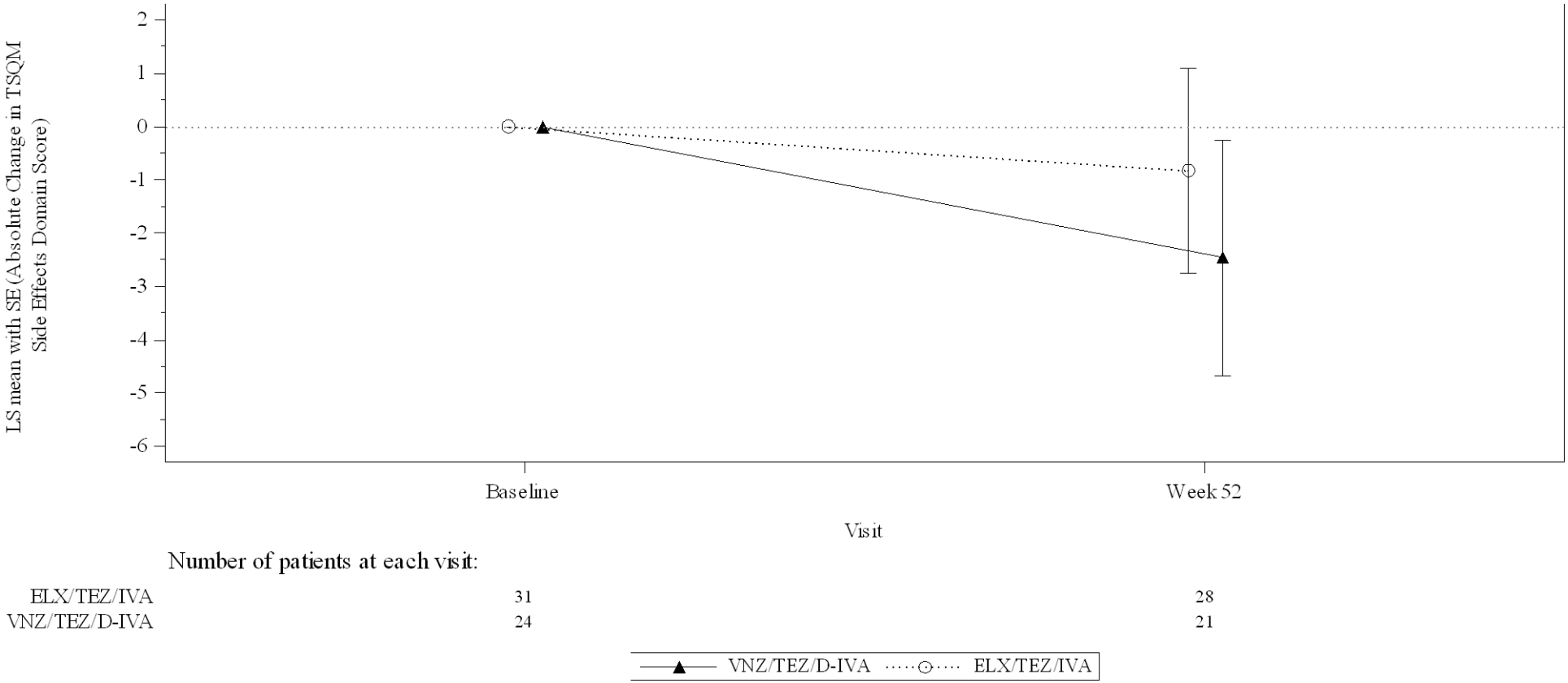
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects



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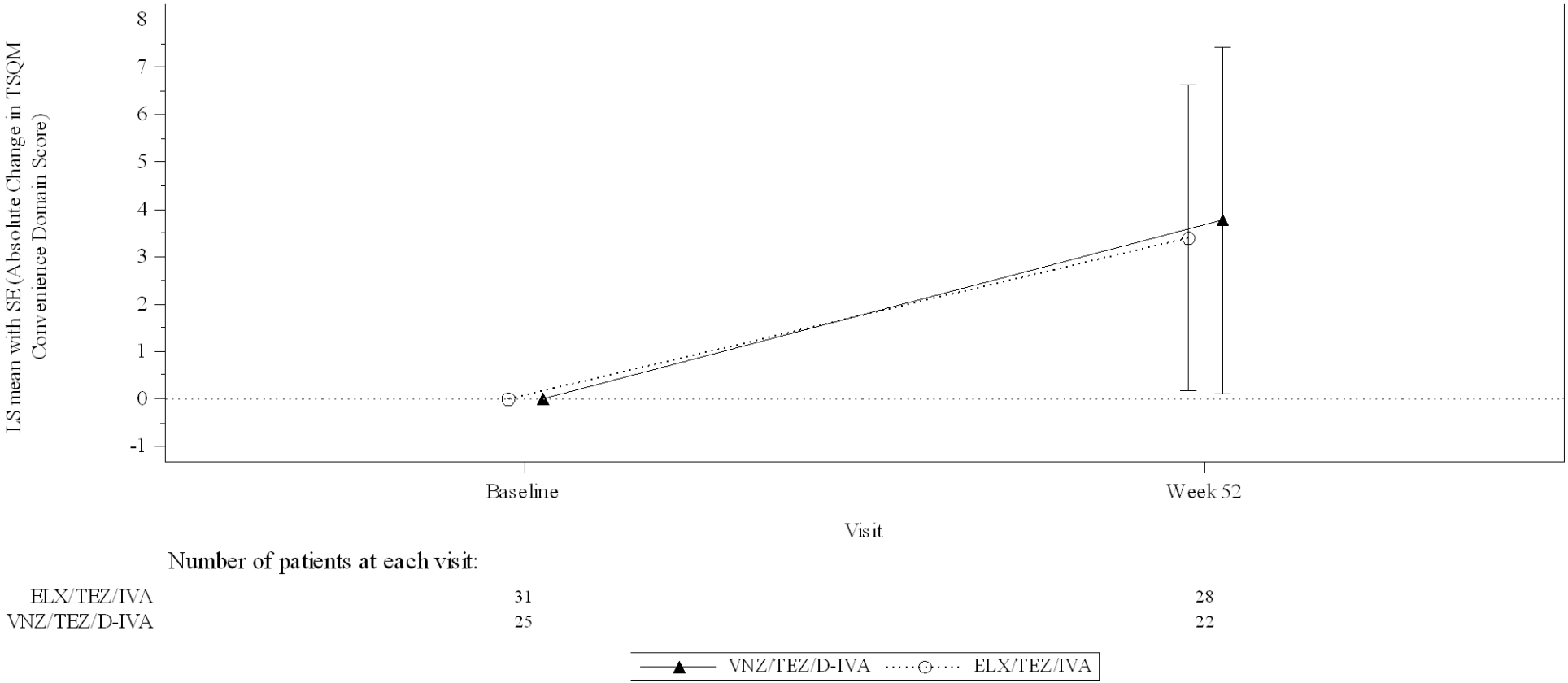
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience



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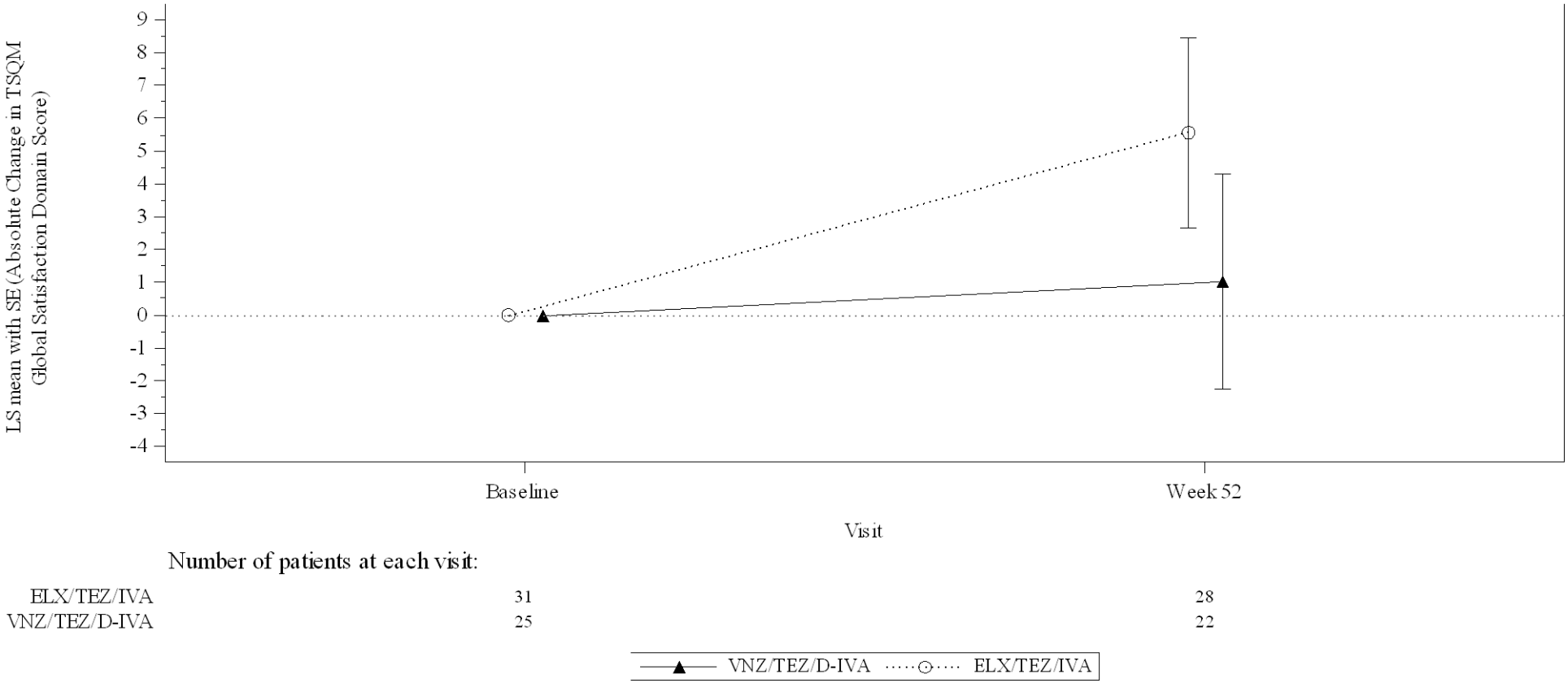
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction



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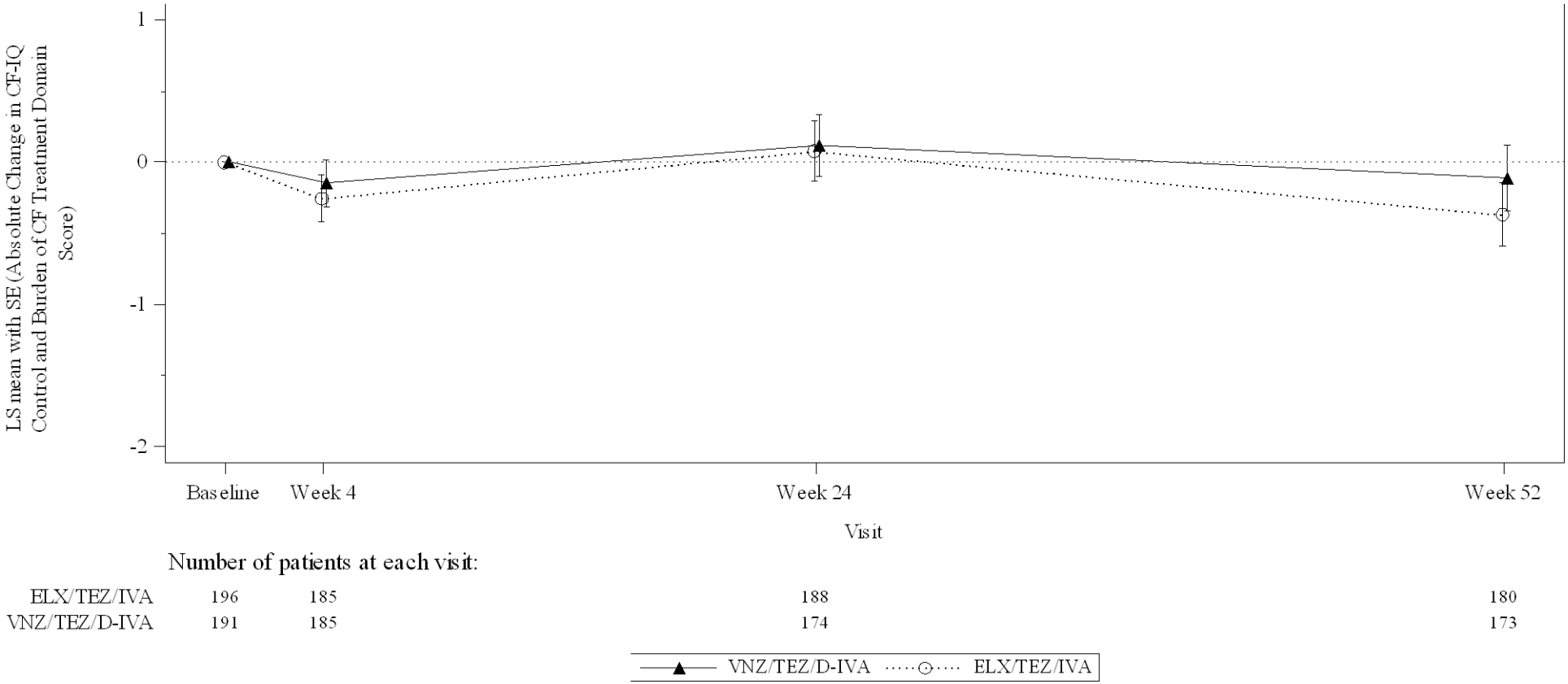
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment



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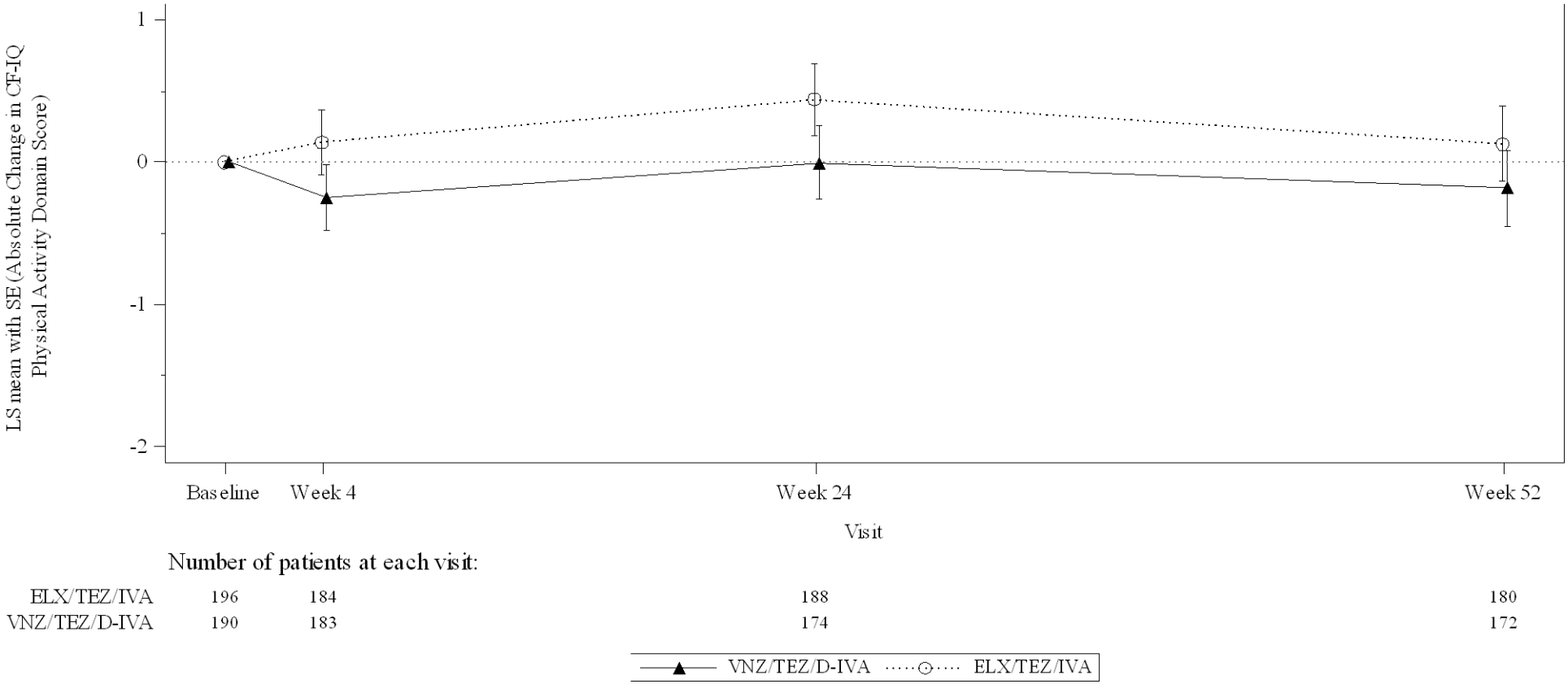
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity



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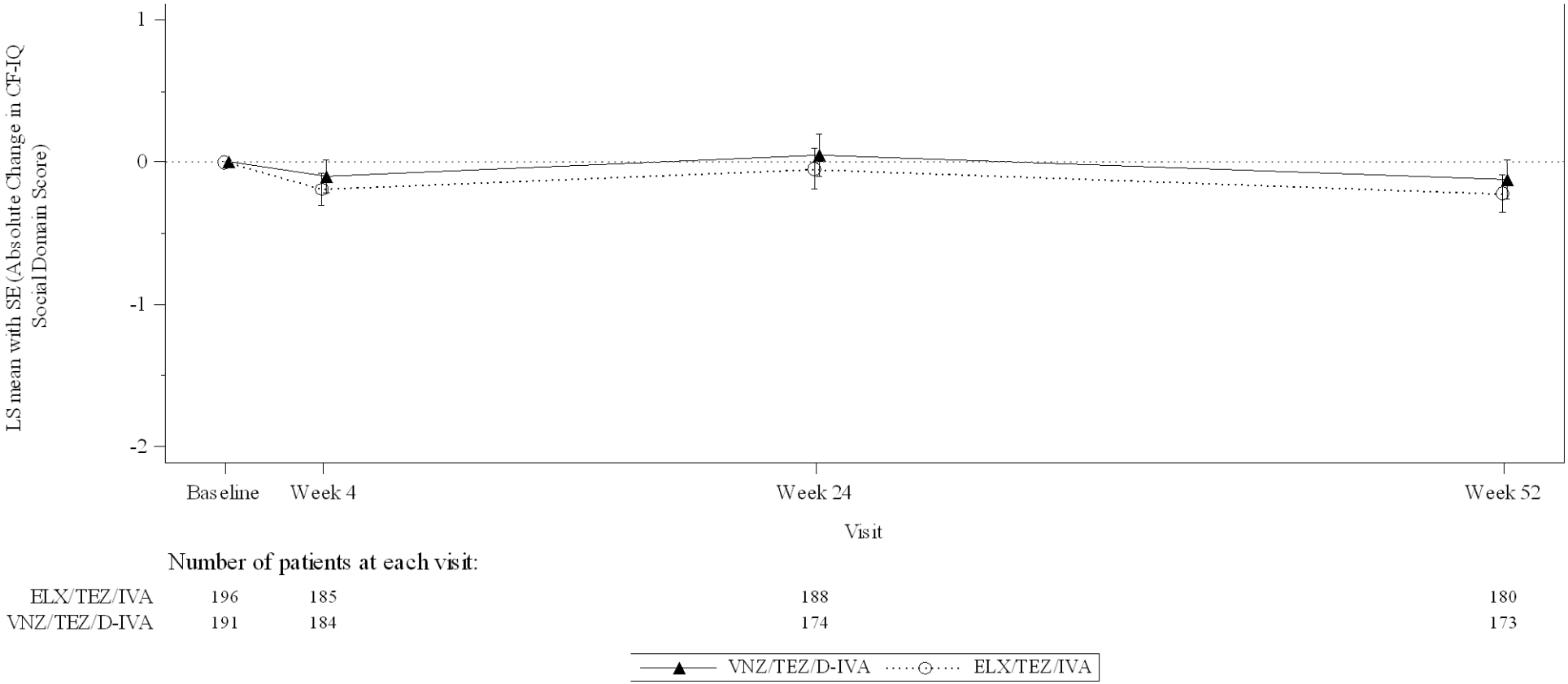
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social



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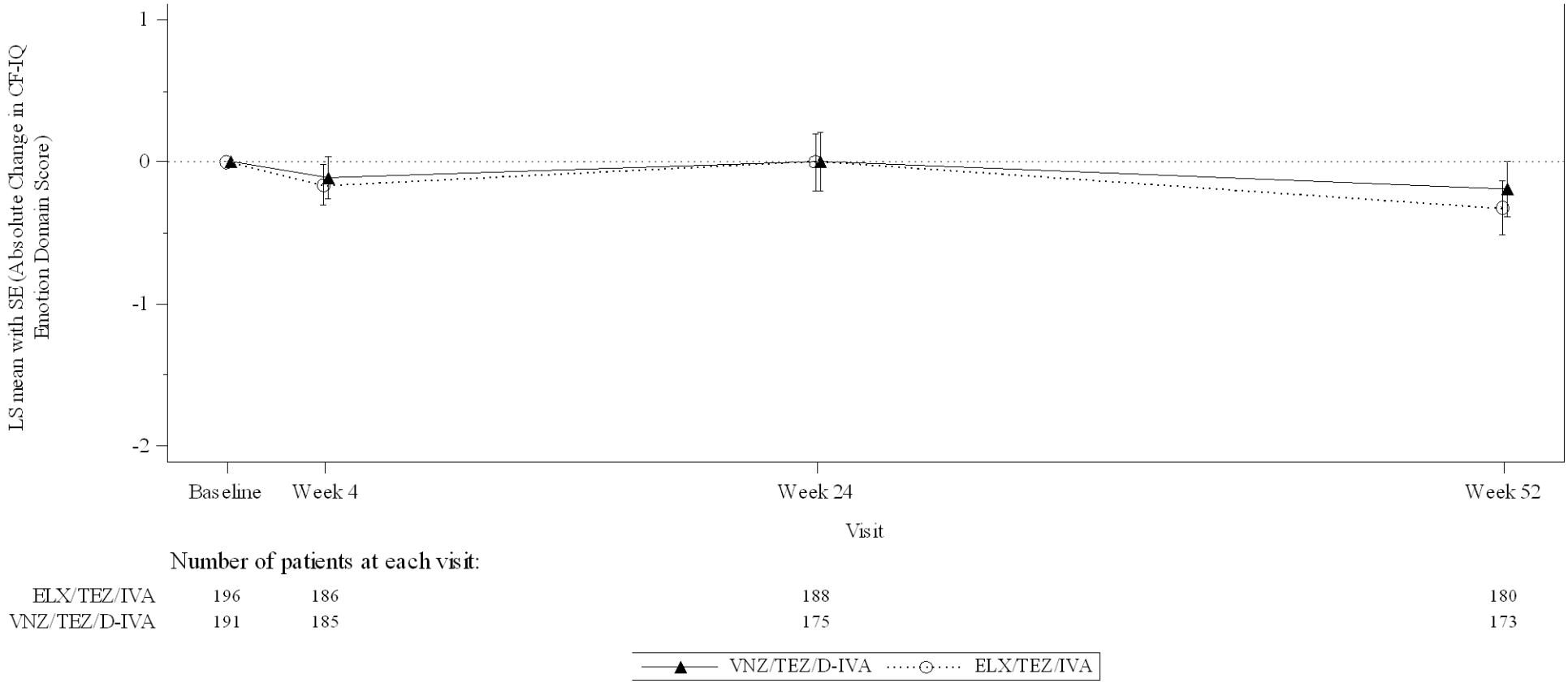
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion



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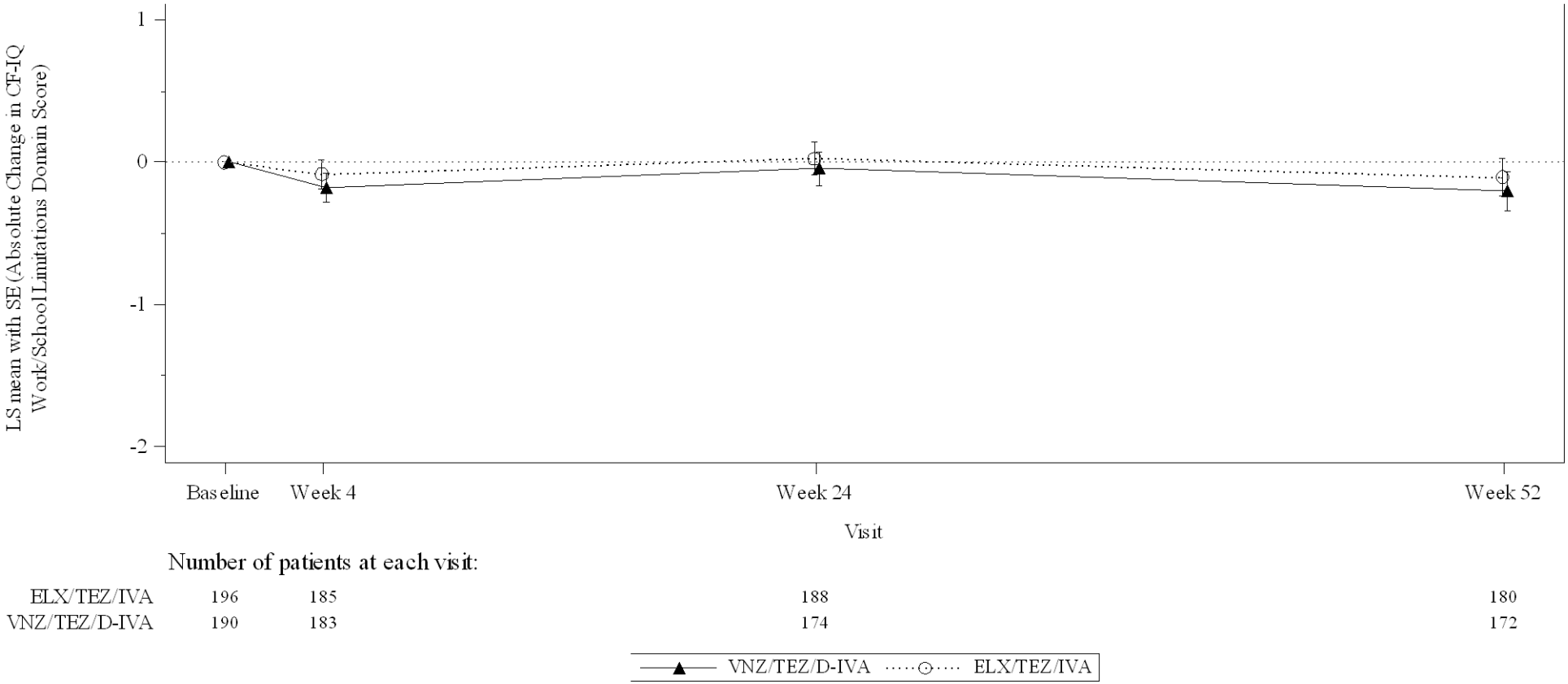
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.1.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations



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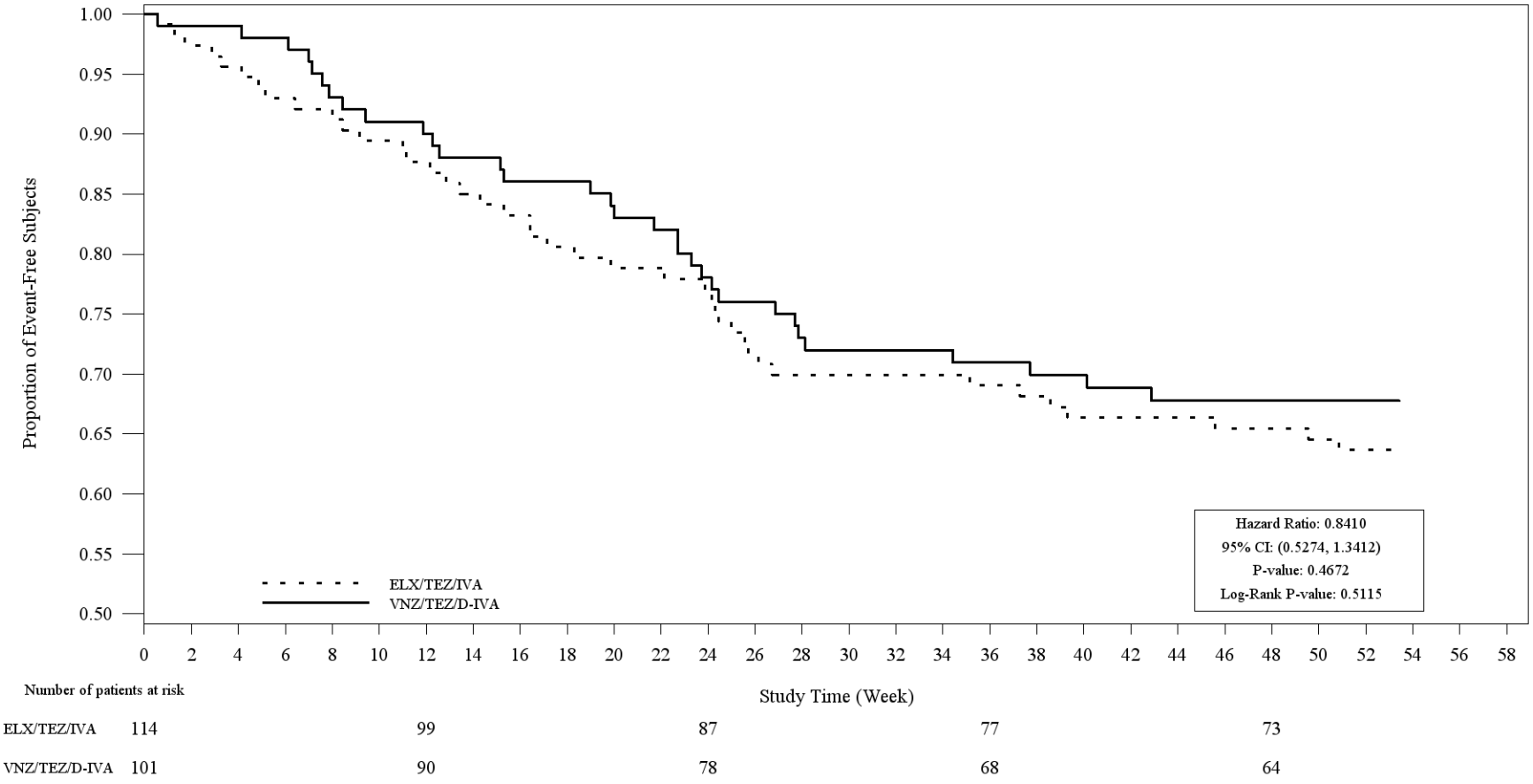
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-102.sas Creation: 17DEC2024 13:47

Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: ppFEV$_1$ at Baseline <70 %

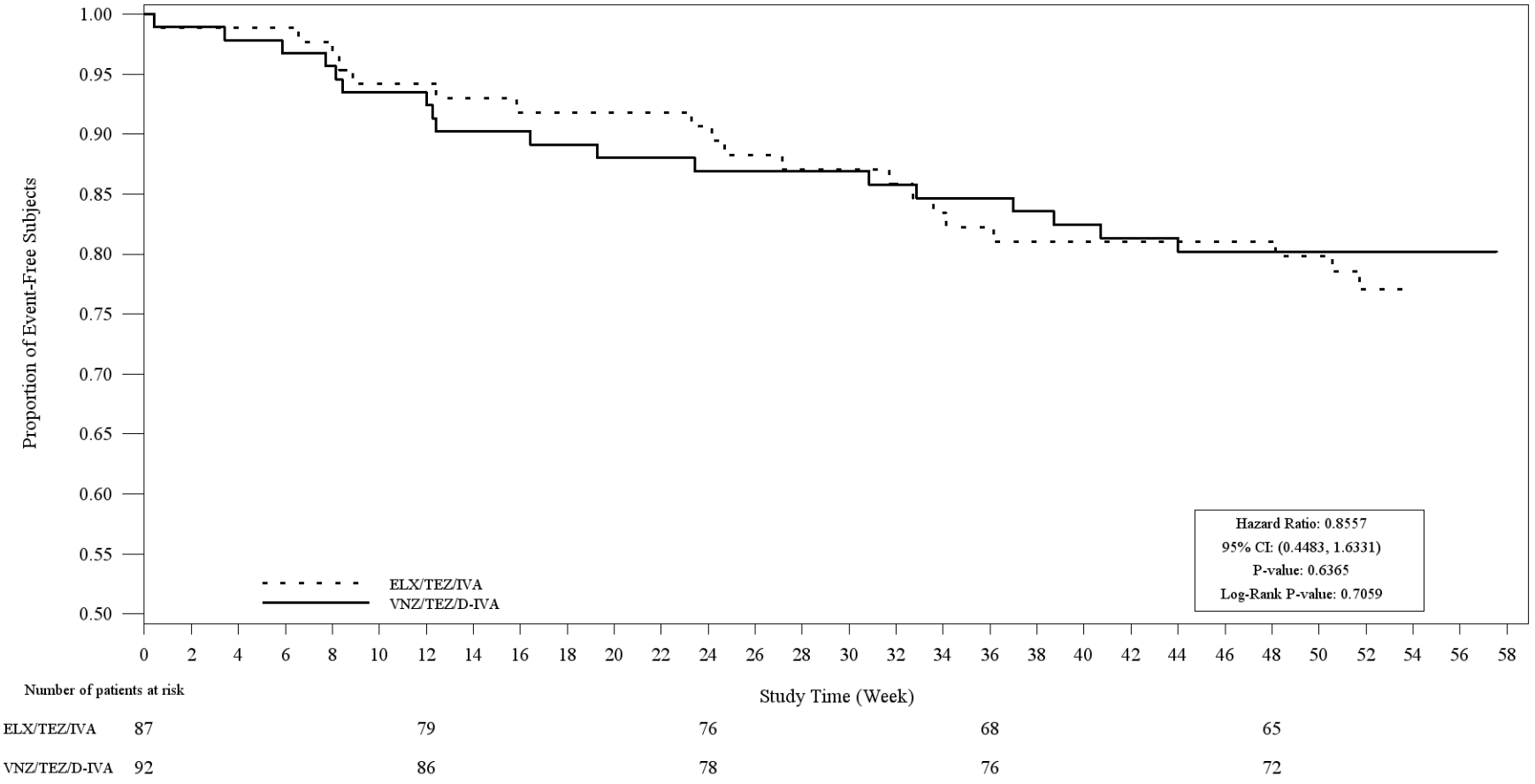


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: ppFEV$_1$ at Baseline ≥70 %



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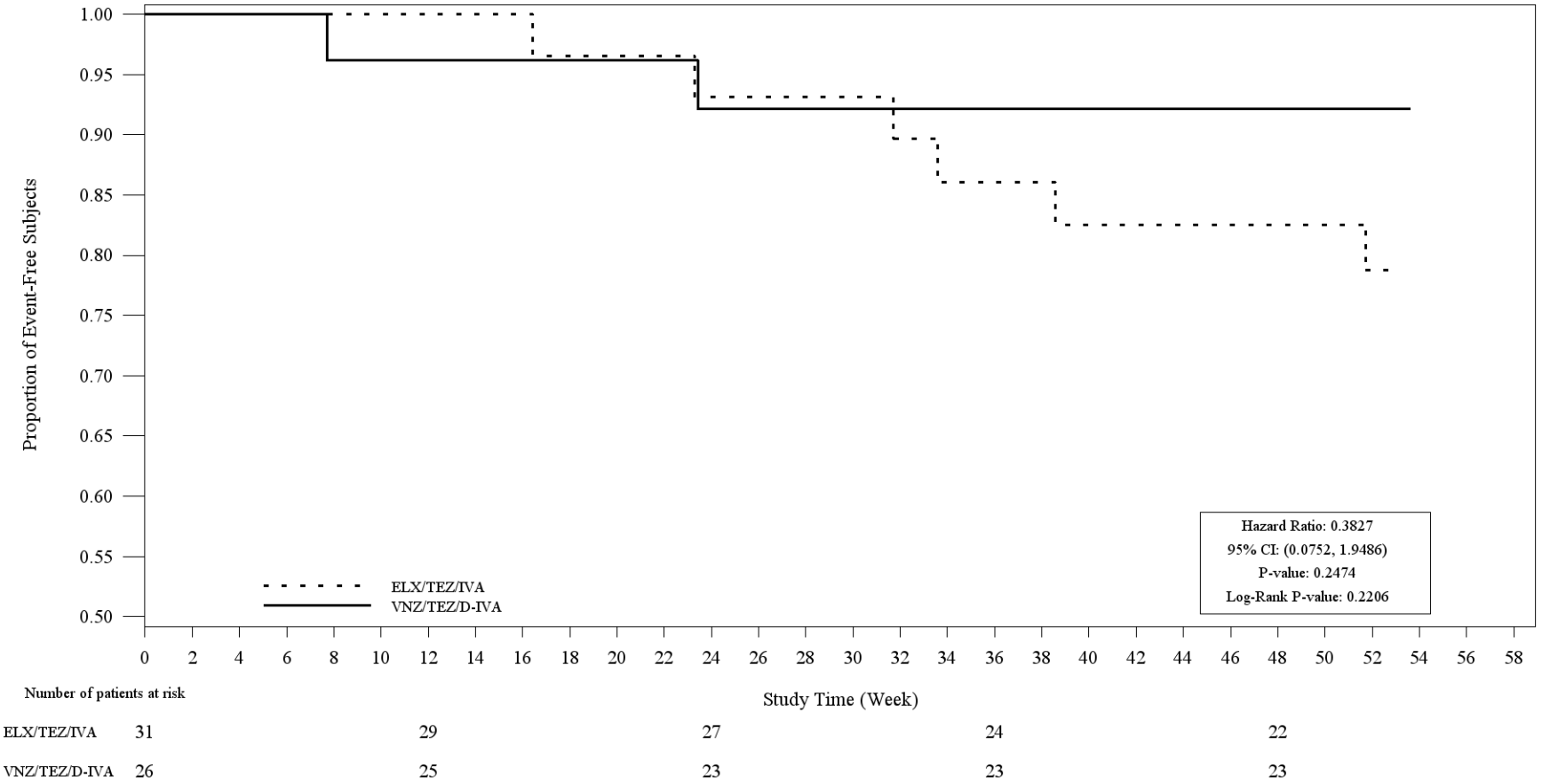
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening < 18 years



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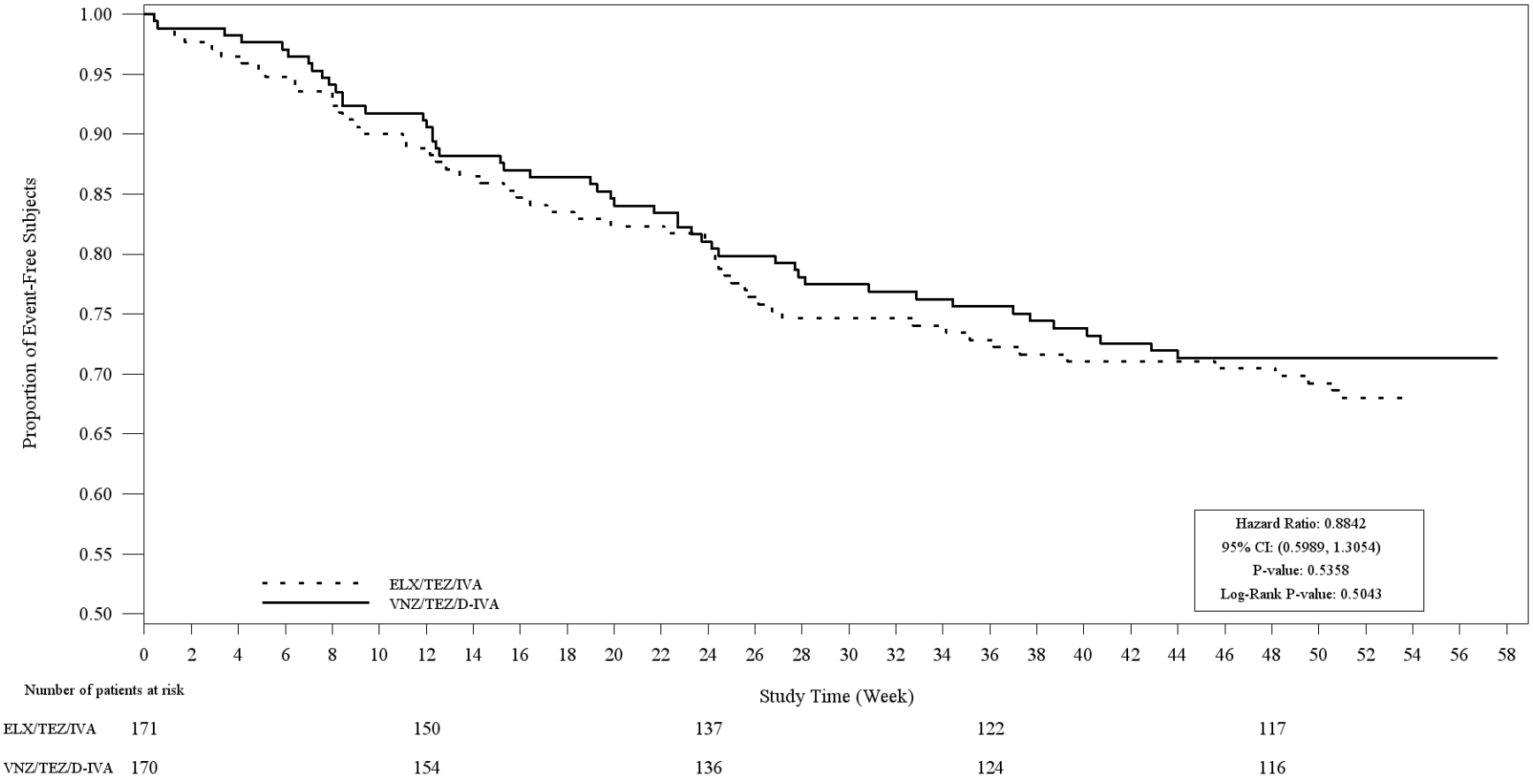
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening ≥ 18 years



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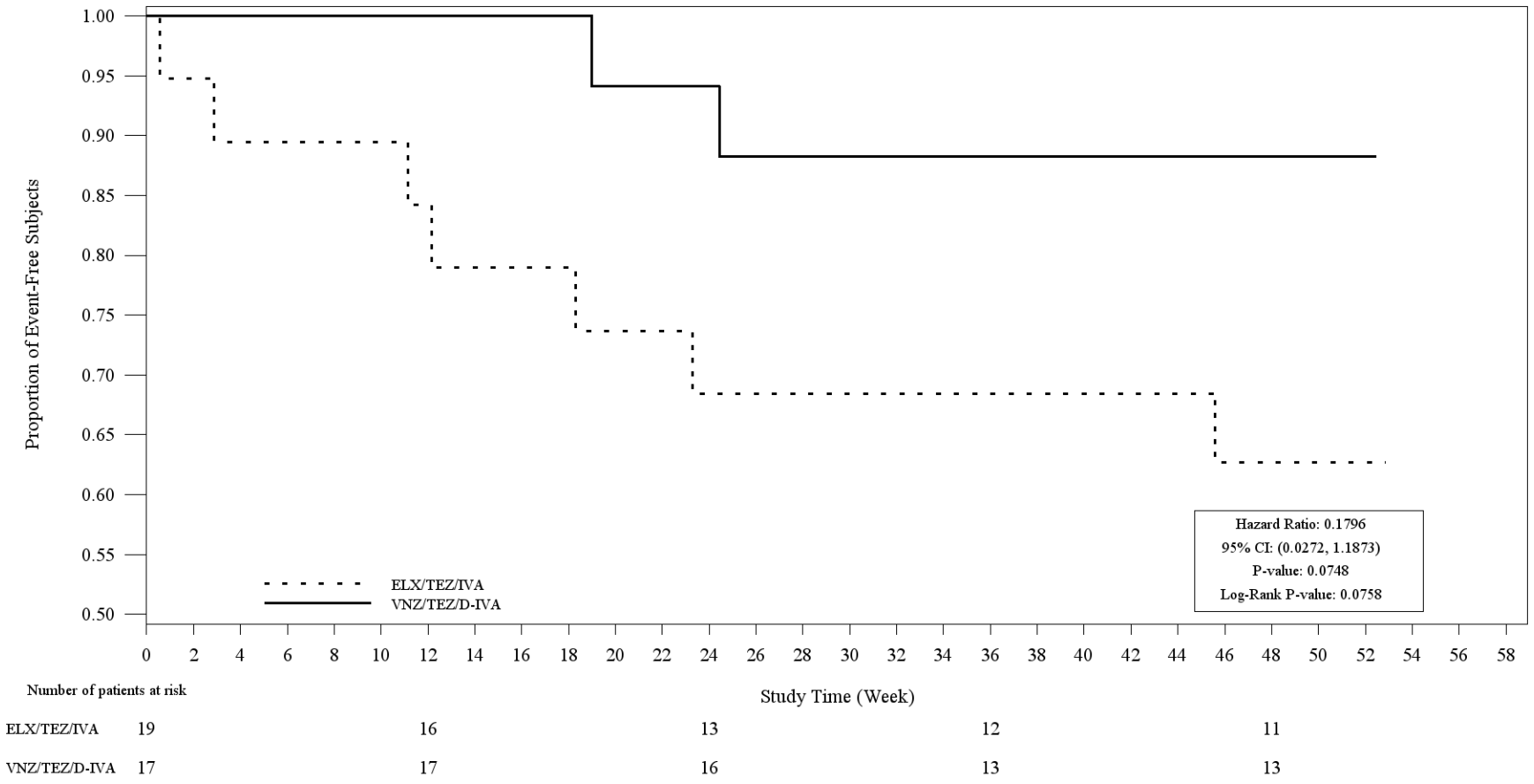
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline <30 mmol/L



Number of patients at risk

ELX/TEZ/IVA	19	16	13	12	11
VNZ/TEZ/D-IVA	17	17	16	13	13

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

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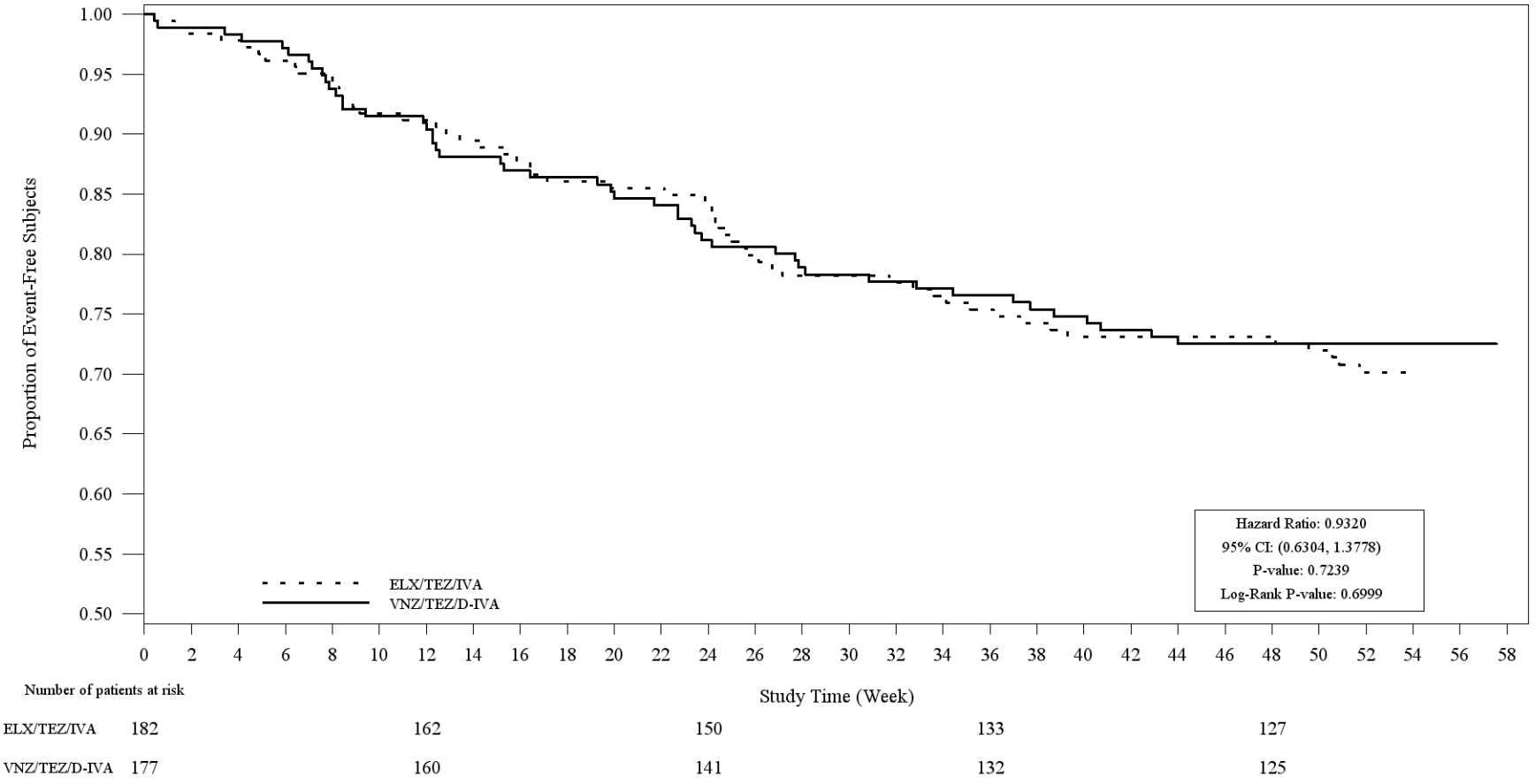
Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline ≥30 mmol/L



Number of patients at risk

ELX/TEZ/IVA	182	162	150	133	127
VNZ/TEZ/D-IVA	177	160	141	132	125

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

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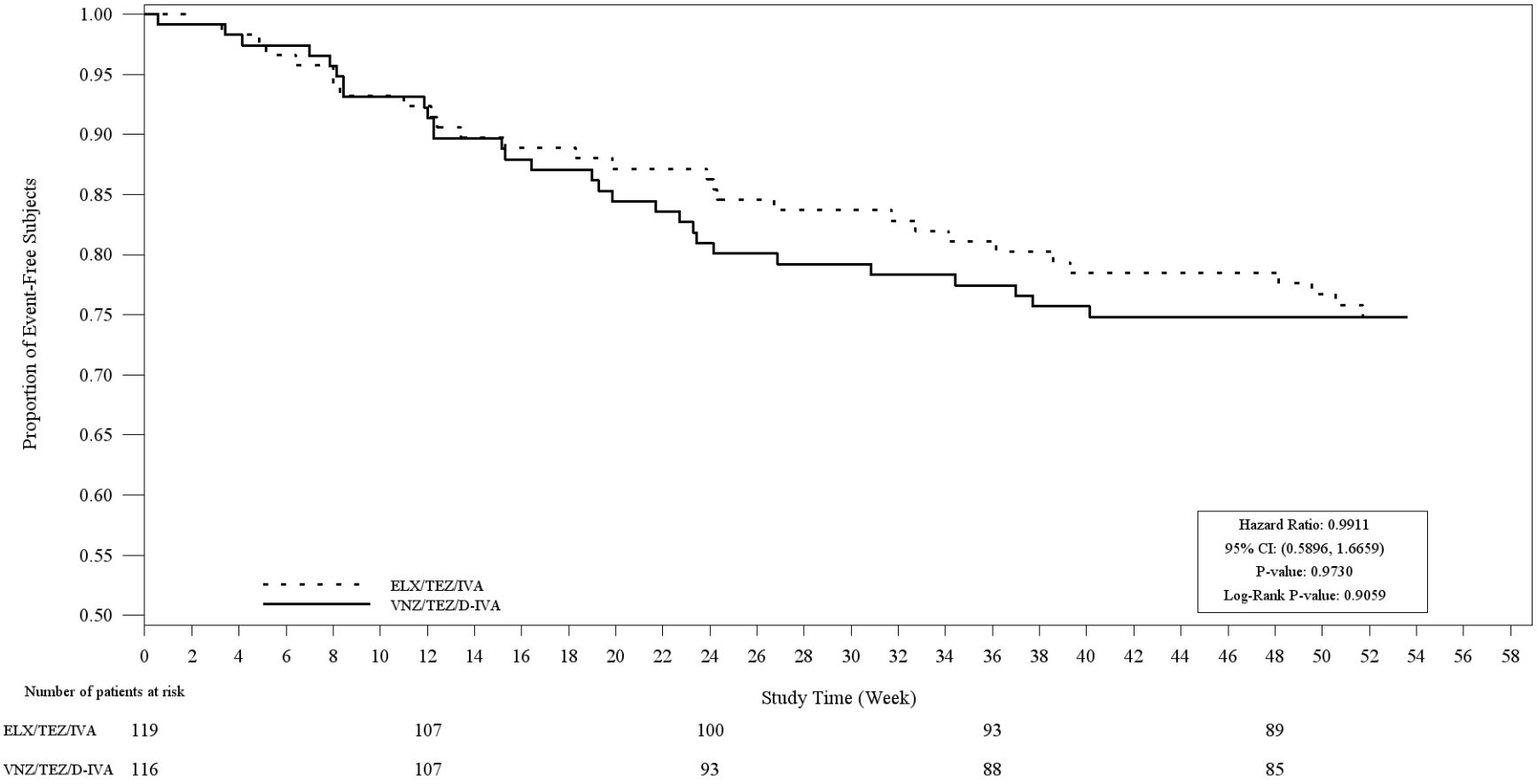
Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Male



Number of patients at risk

ELX/TEZ/IVA	119	107	100	93	89
VNZ/TEZ/D-IVA	116	107	93	88	85

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

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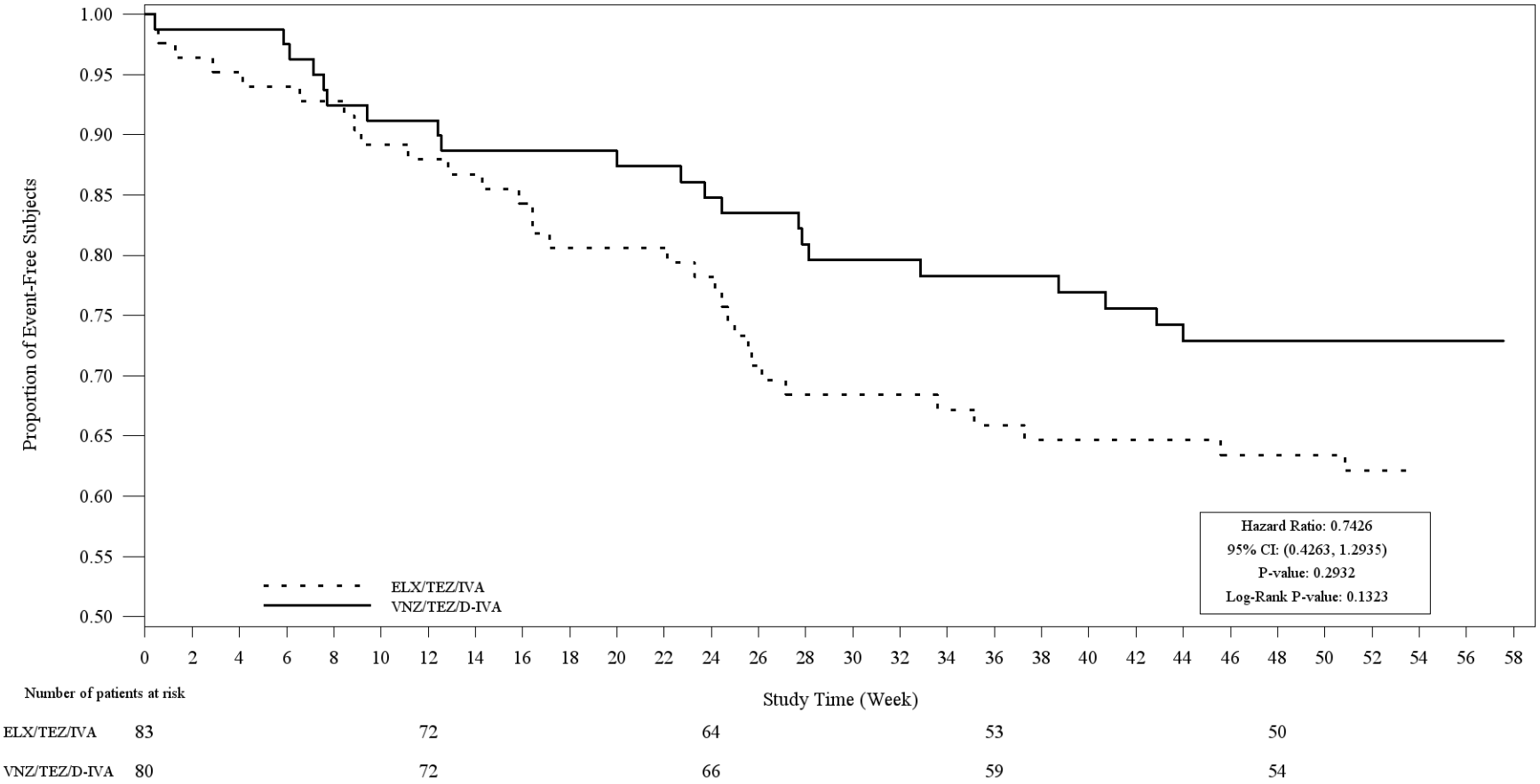
Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Female

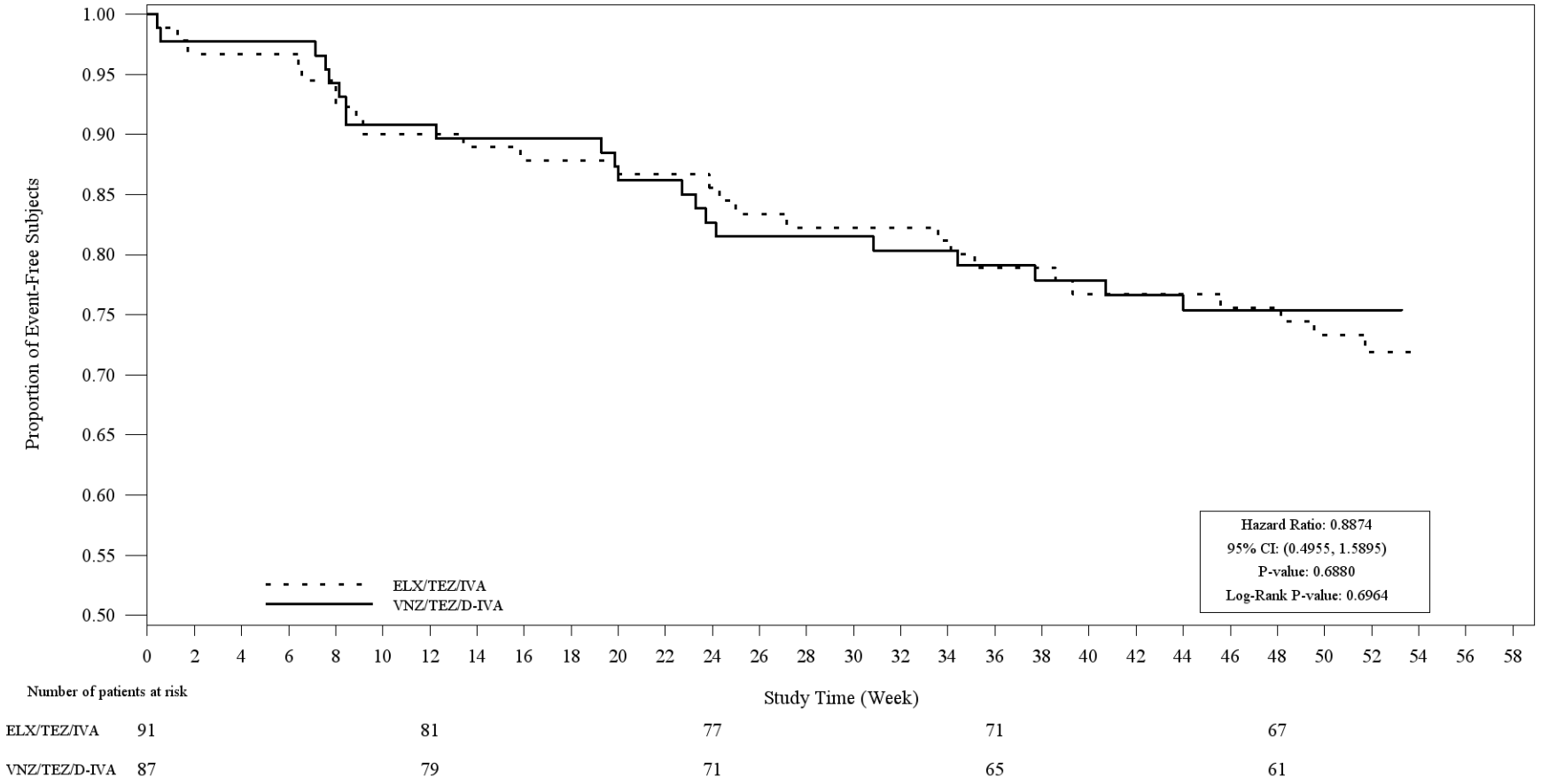


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = North America



Number of patients at risk

ELX/TEZ/IVA	91	81	77	71	67
VNZ/TEZ/D-IVA	87	79	71	65	61

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

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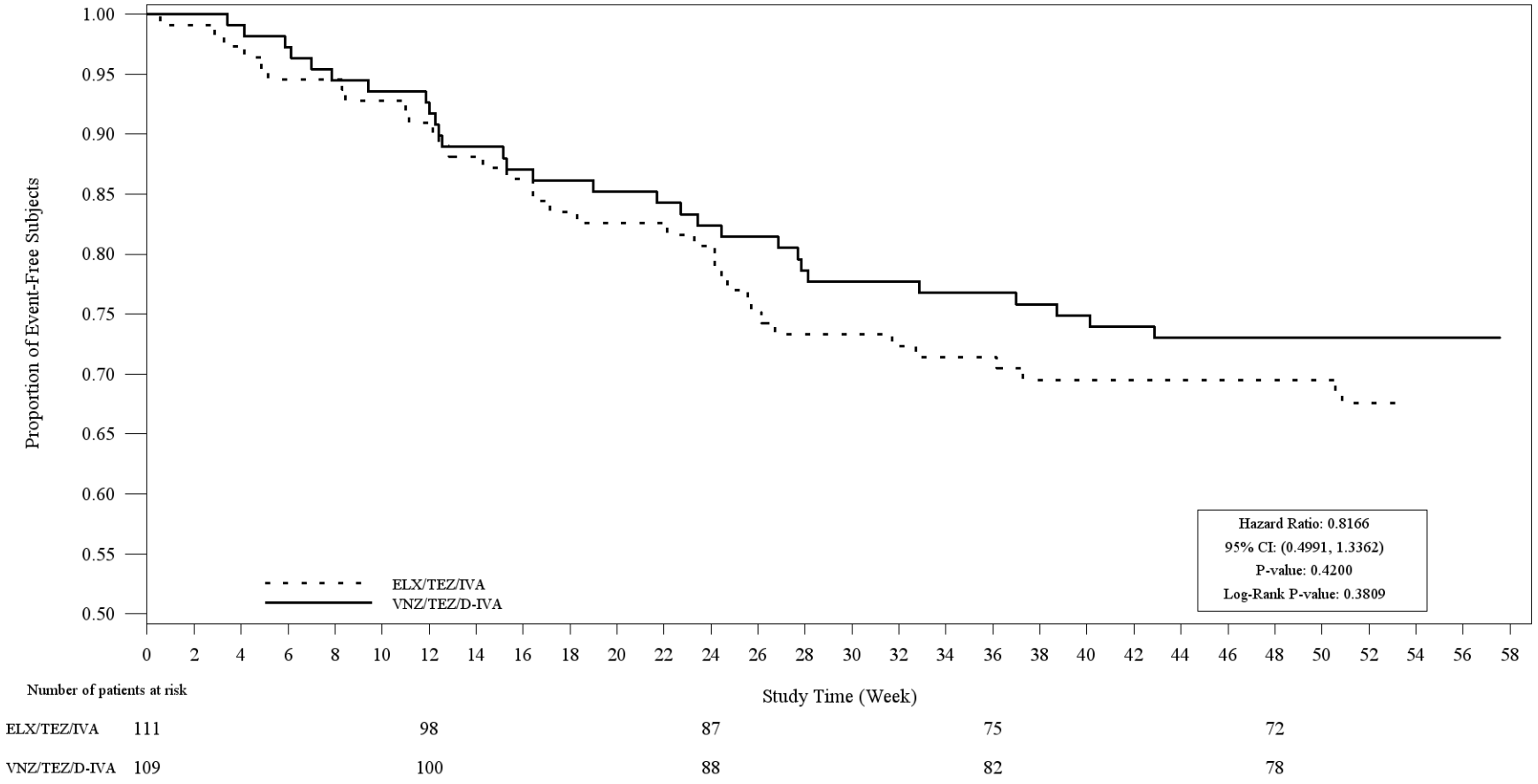
Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = Rest of the World



Number of patients at risk

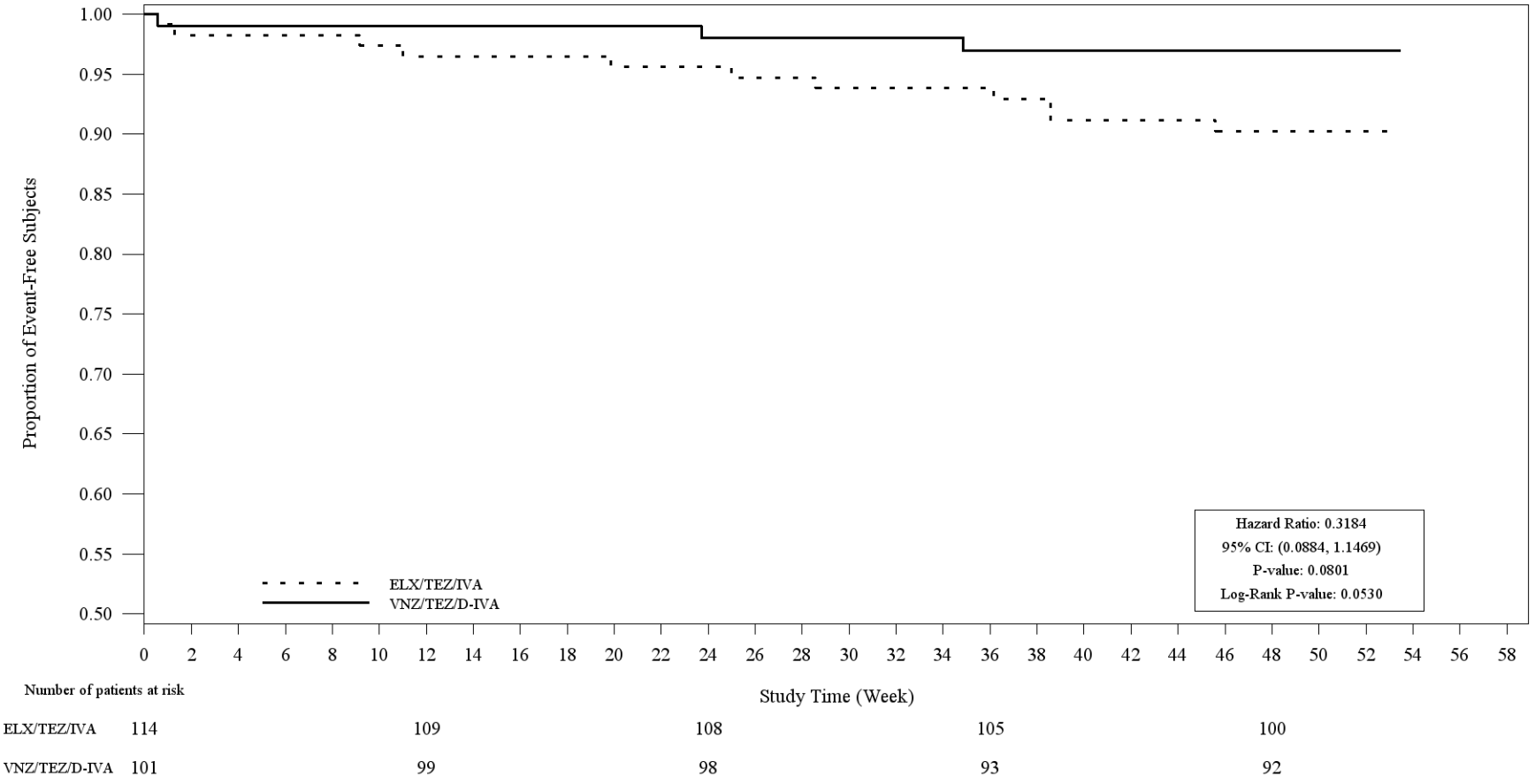
ELX/TEZ/IVA	111	98	87	75	72
VNZ/TEZ/D-IVA	109	100	88	82	78

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: ppFEV$_1$ at Baseline <70 %



Number of patients at risk

ELX/TEZ/IVA	114	109	108	105	100
VNZ/TEZ/D-IVA	101	99	98	93	92

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

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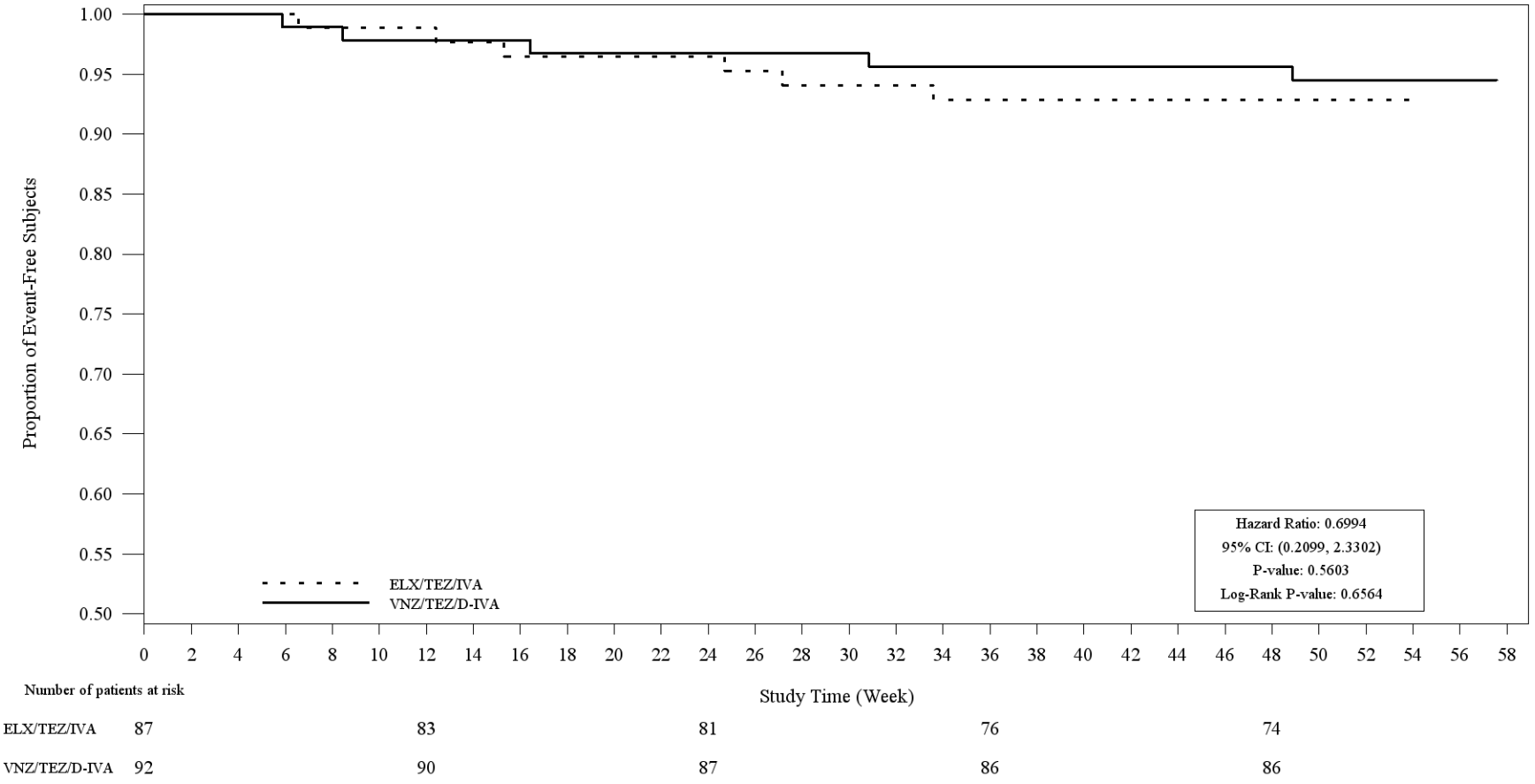
Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: ppFEV$_1$ at Baseline ≥70 %



Number of patients at risk

ELX/TEZ/IVA	87	83	81	76	74
VNZ/TEZ/D-IVA	92	90	87	86	86

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

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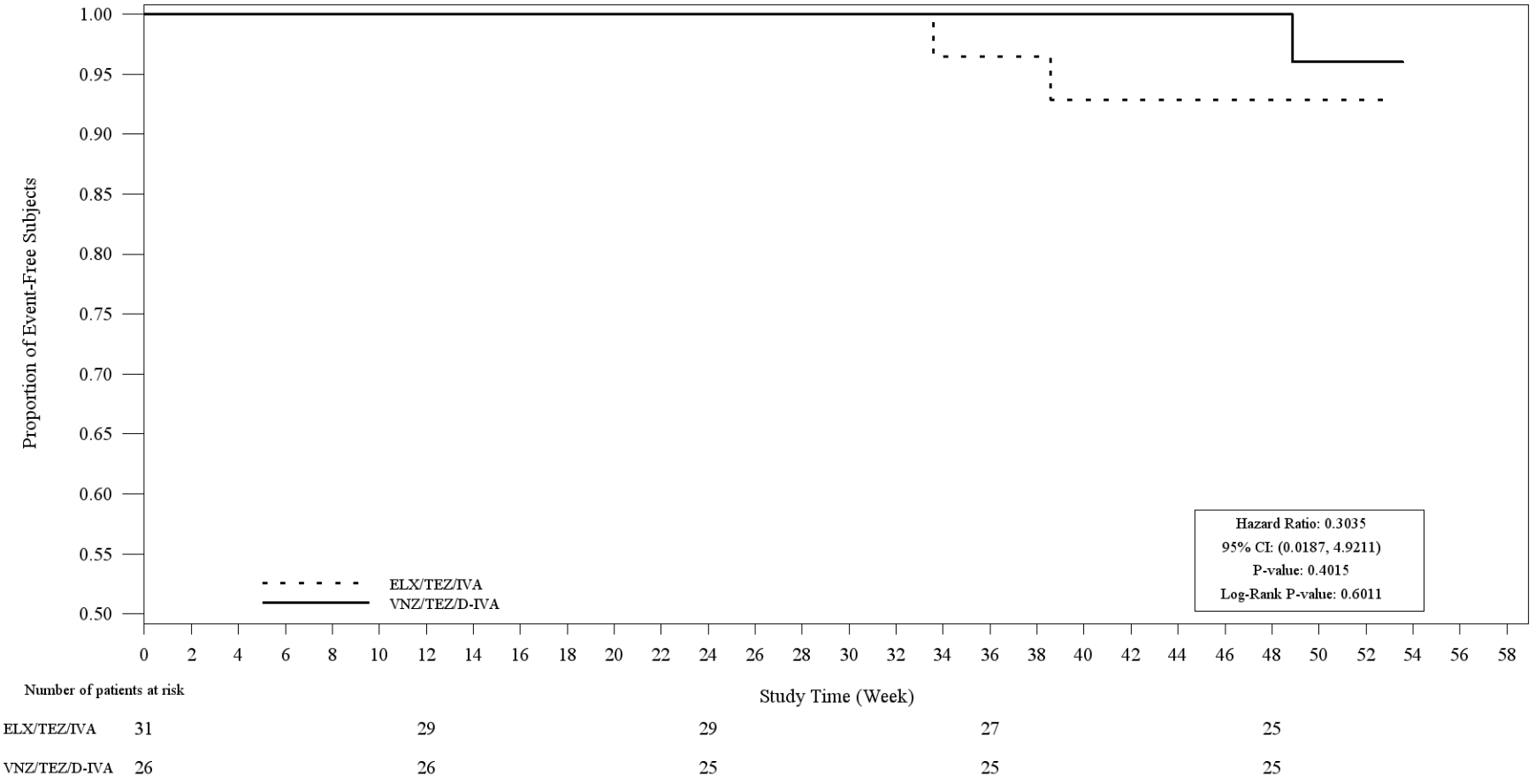
Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening < 18 years

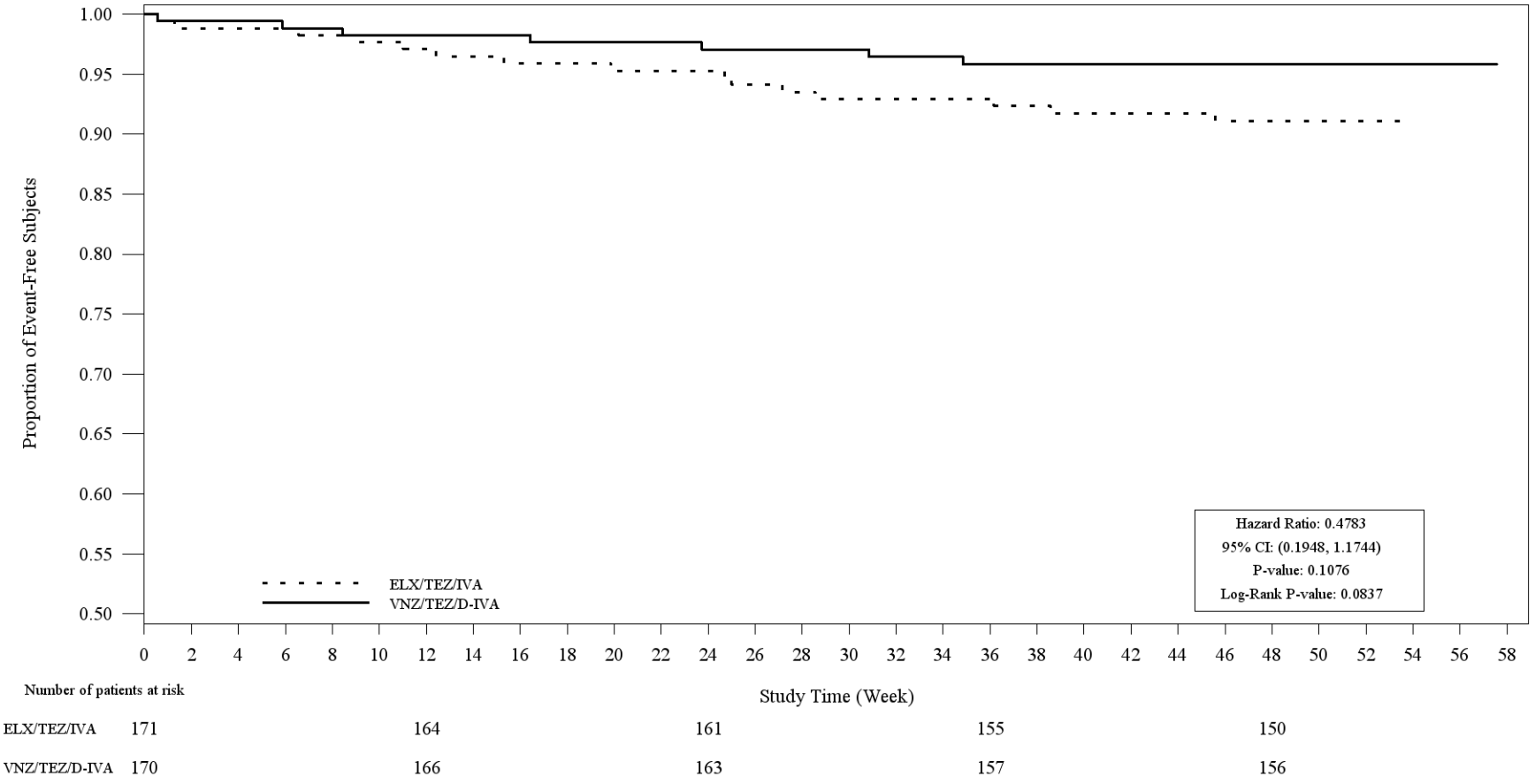


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-hosp-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening ≥ 18 years



Number of patients at risk

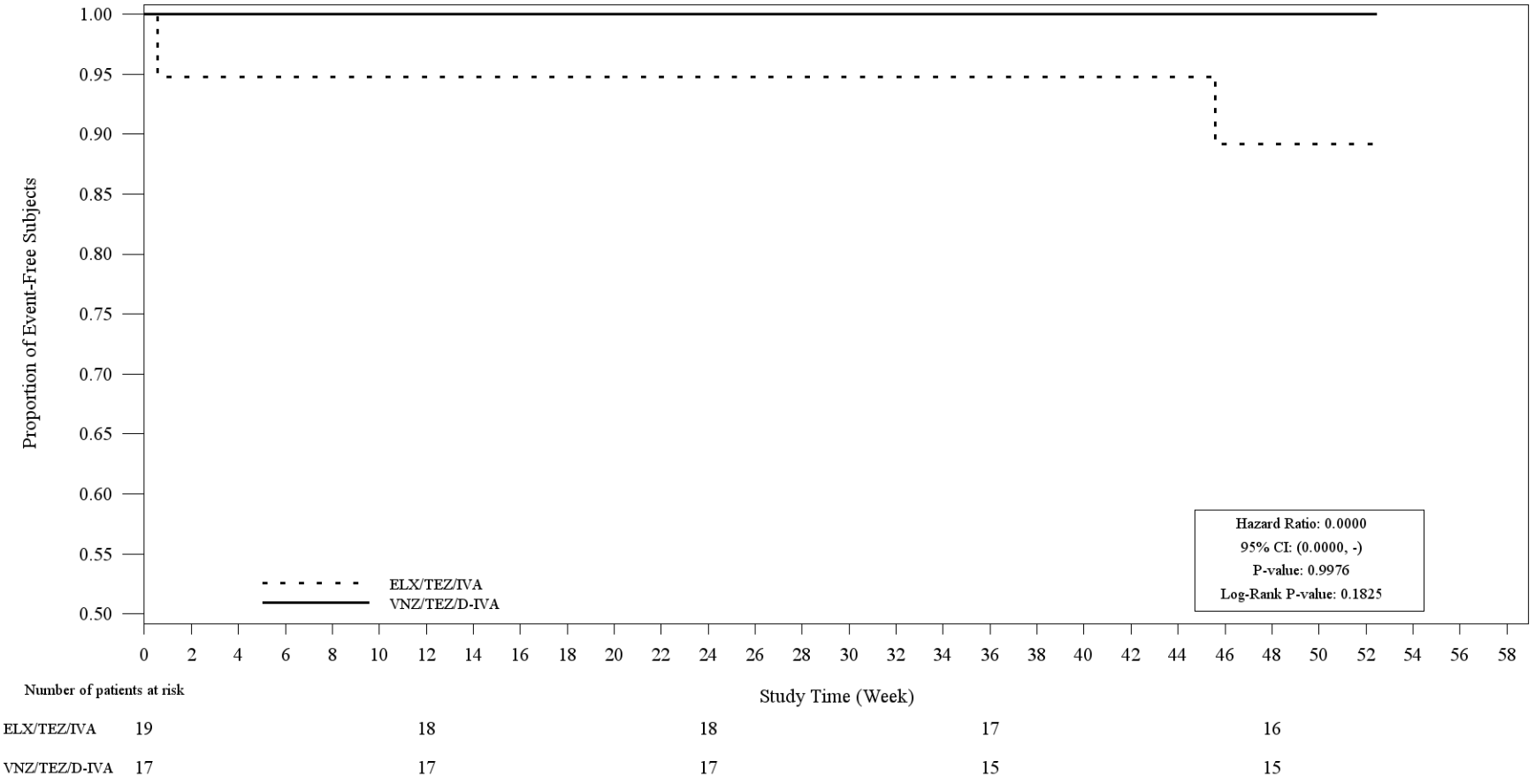
ELX/TEZ/IVA	171	164	161	155	150
VNZ/TEZ/D-IVA	170	166	163	157	156

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-hosp-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline <30 mmol/L



Number of patients at risk

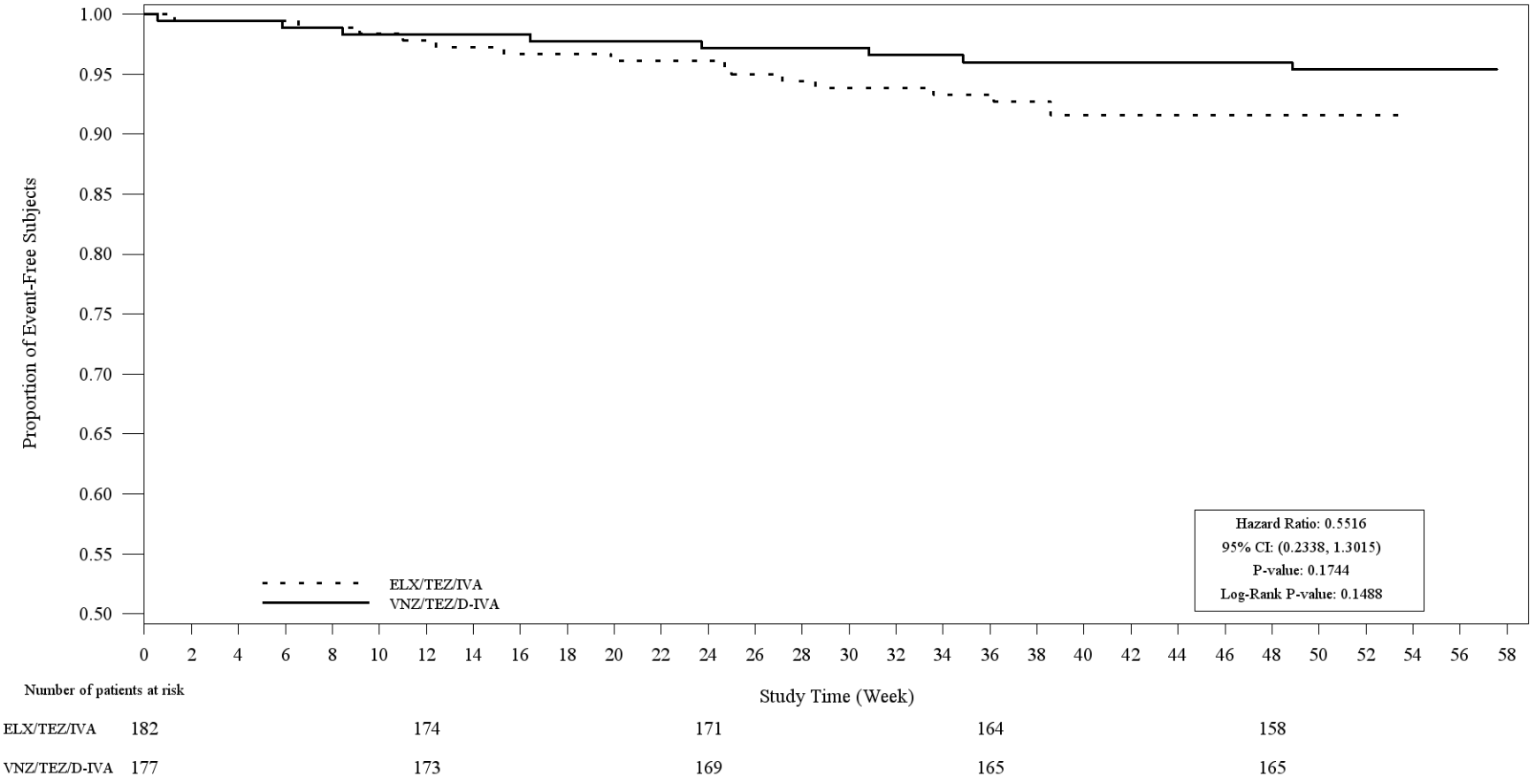
ELX/TEZ/IVA	19	18	18	17	16
VNZ/TEZ/D-IVA	17	17	17	15	15

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-hosp-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline ≥30 mmol/L



Number of patients at risk

ELX/TEZ/IVA	182	174	171	164	158
VNZ/TEZ/D-IVA	177	173	169	165	165

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

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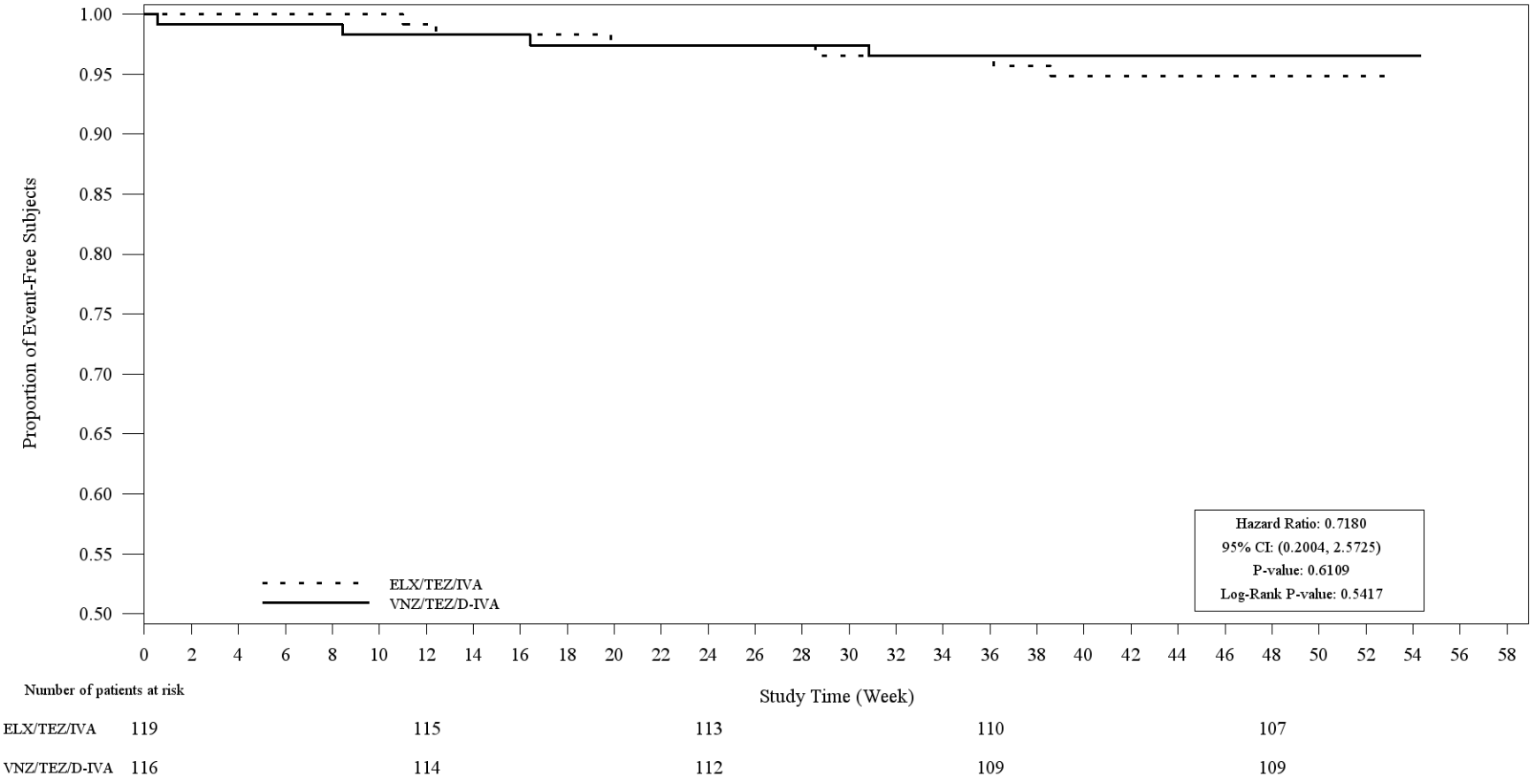
Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Male

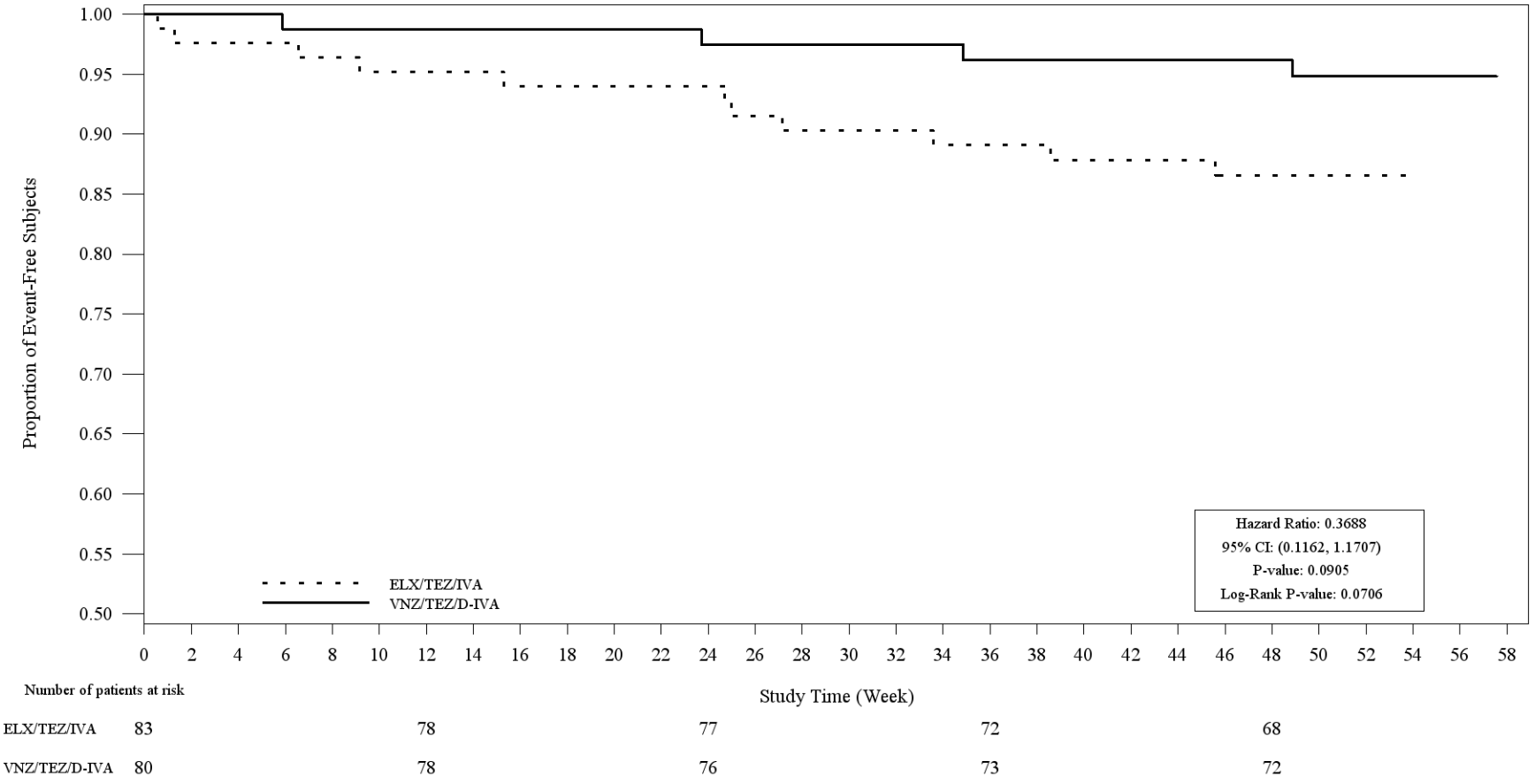


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-hosp-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Female

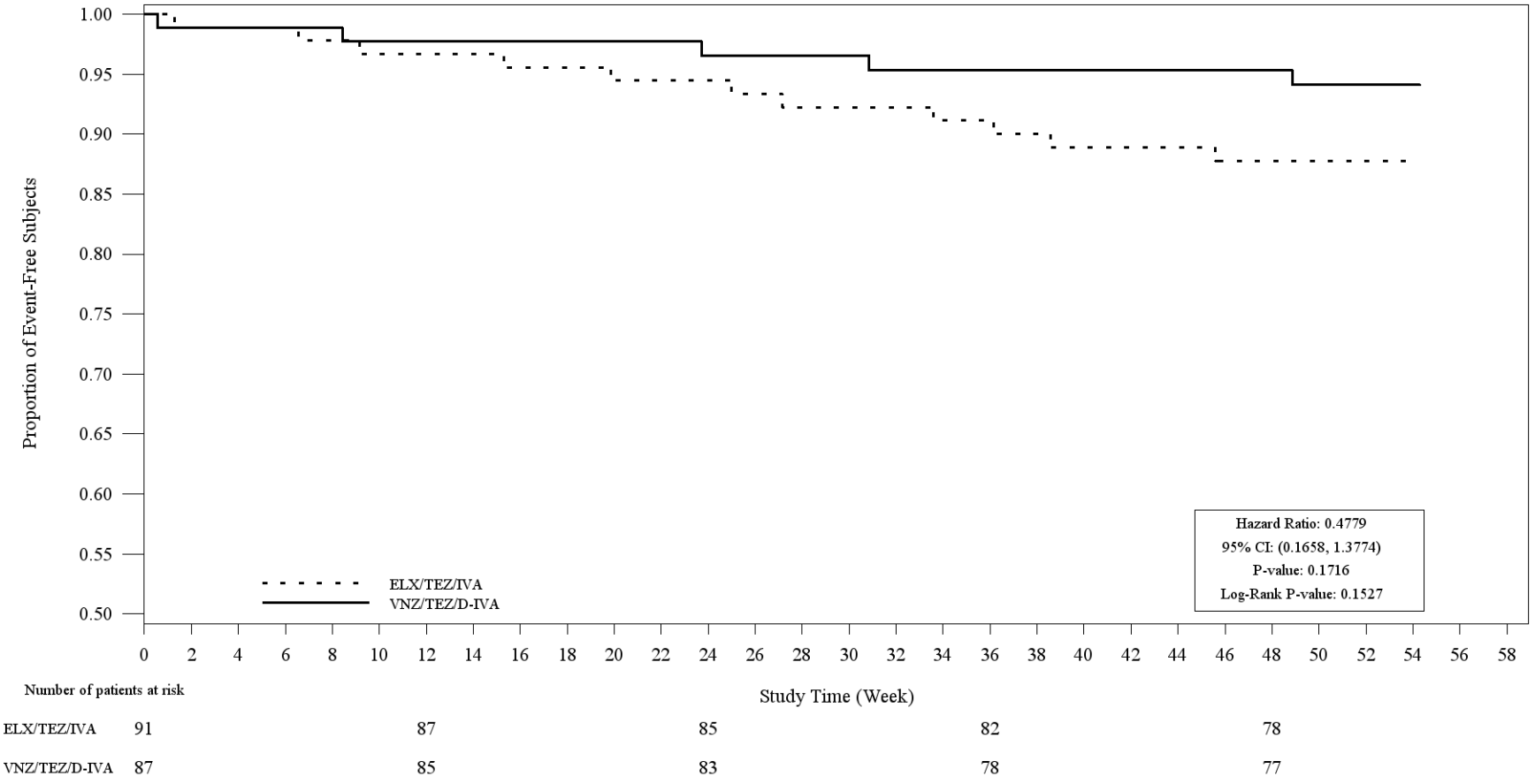


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-hosp-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = North America

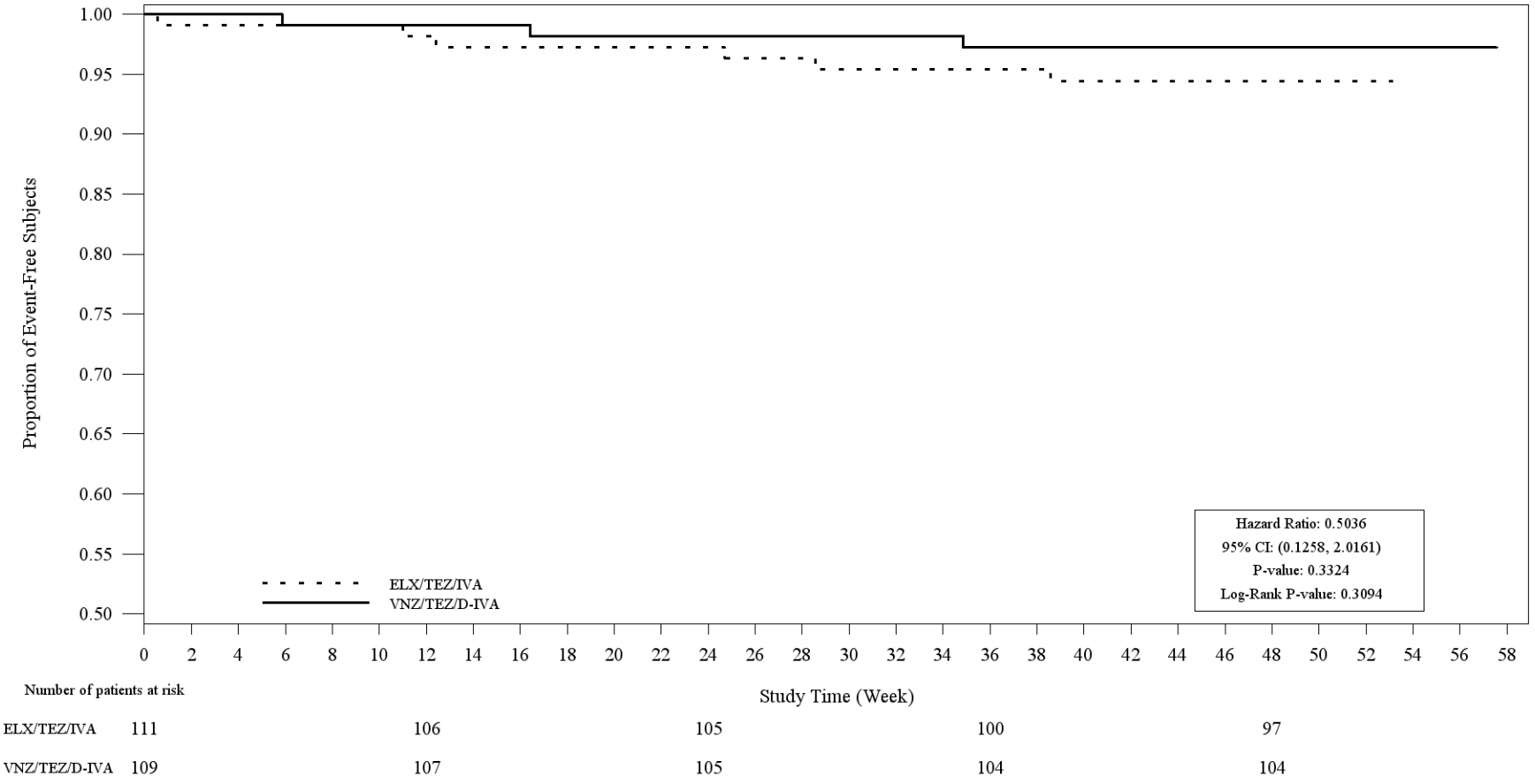


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-hosp-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = Rest of the World



Number of patients at risk

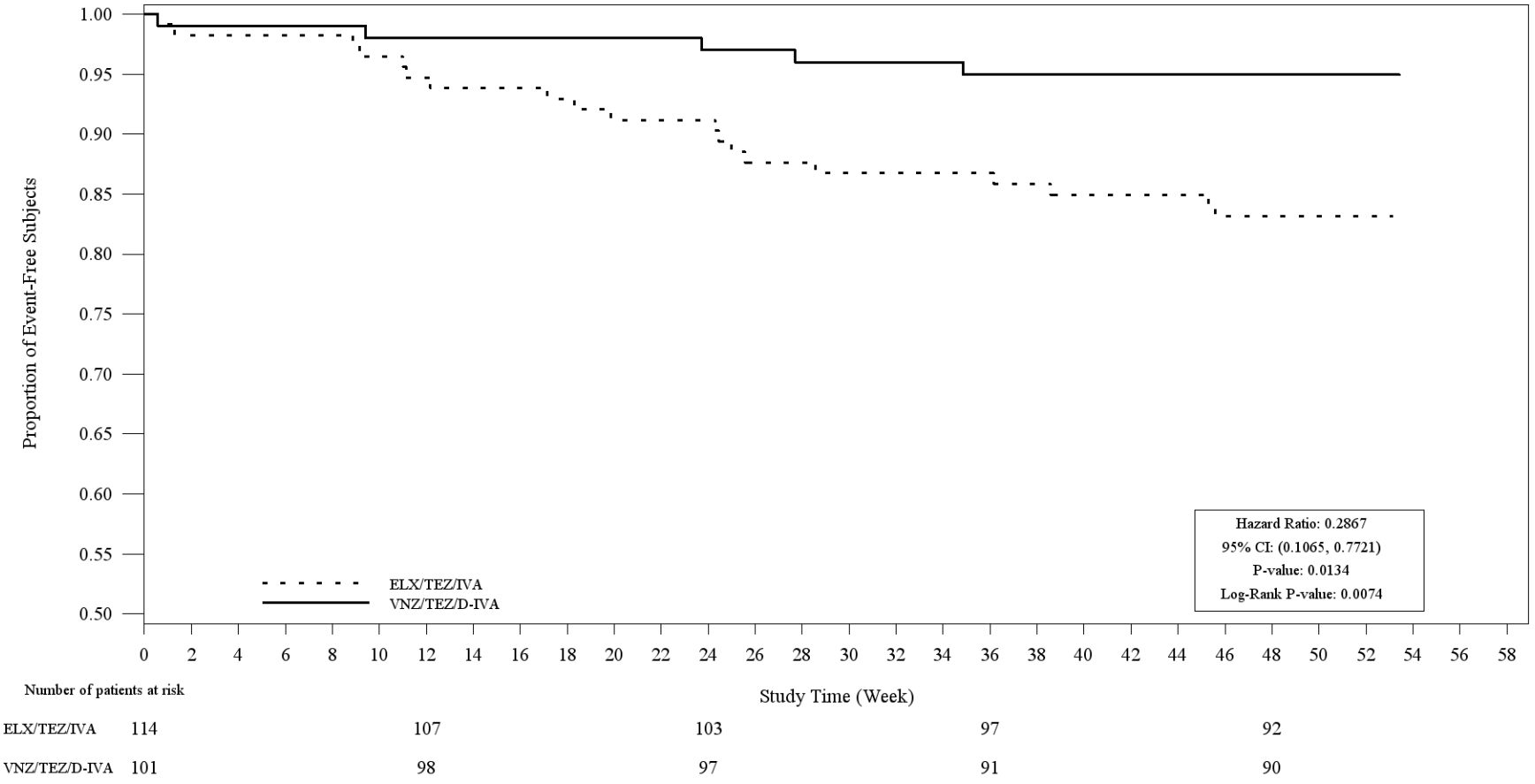
ELX/TEZ/IVA	111	106	105	100	97
VNZ/TEZ/D-IVA	109	107	105	104	104

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-hosp-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: ppFEV$_1$ at Baseline <70 %

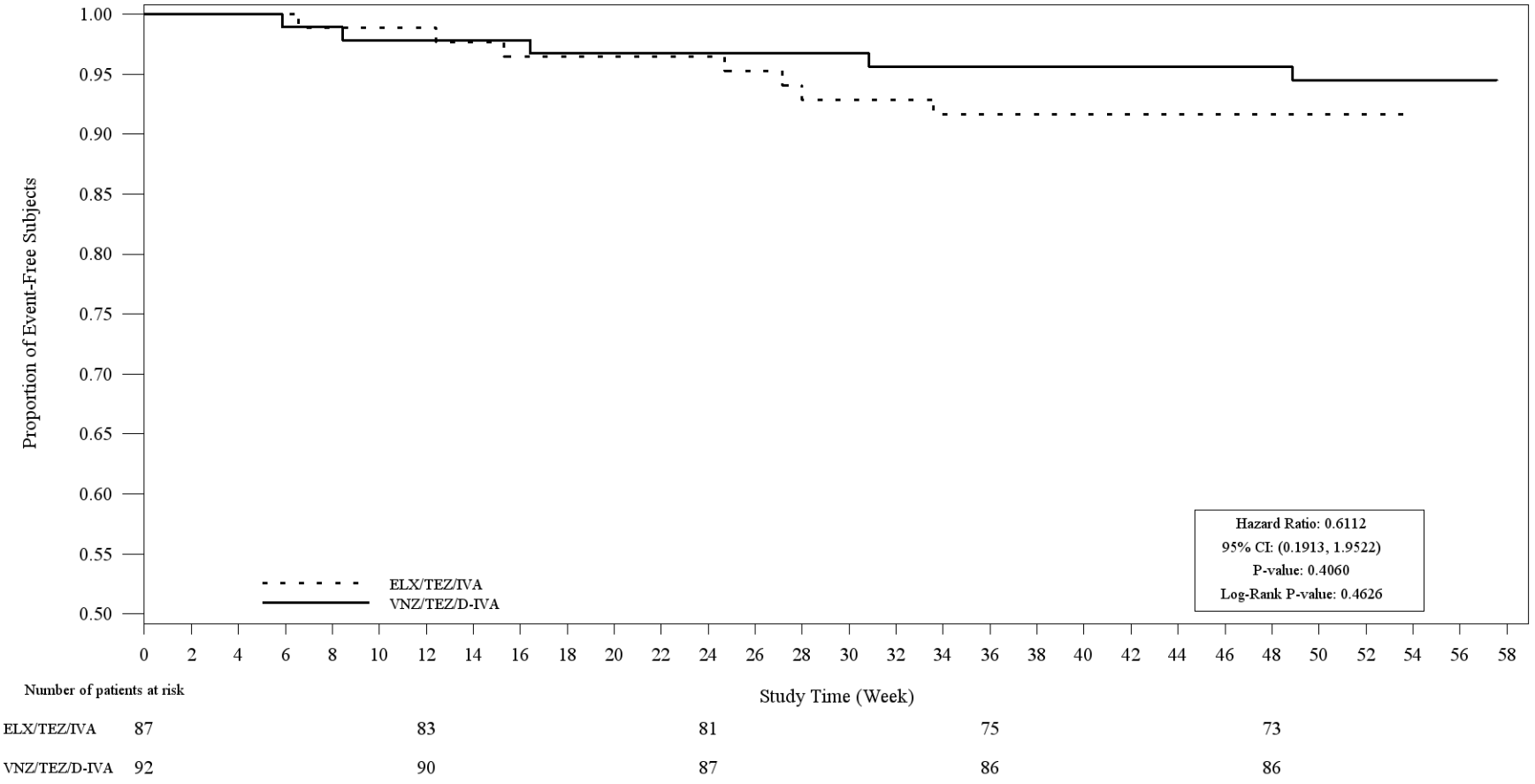


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-iv-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: ppFEV$_1$ at Baseline ≥70 %



Number of patients at risk

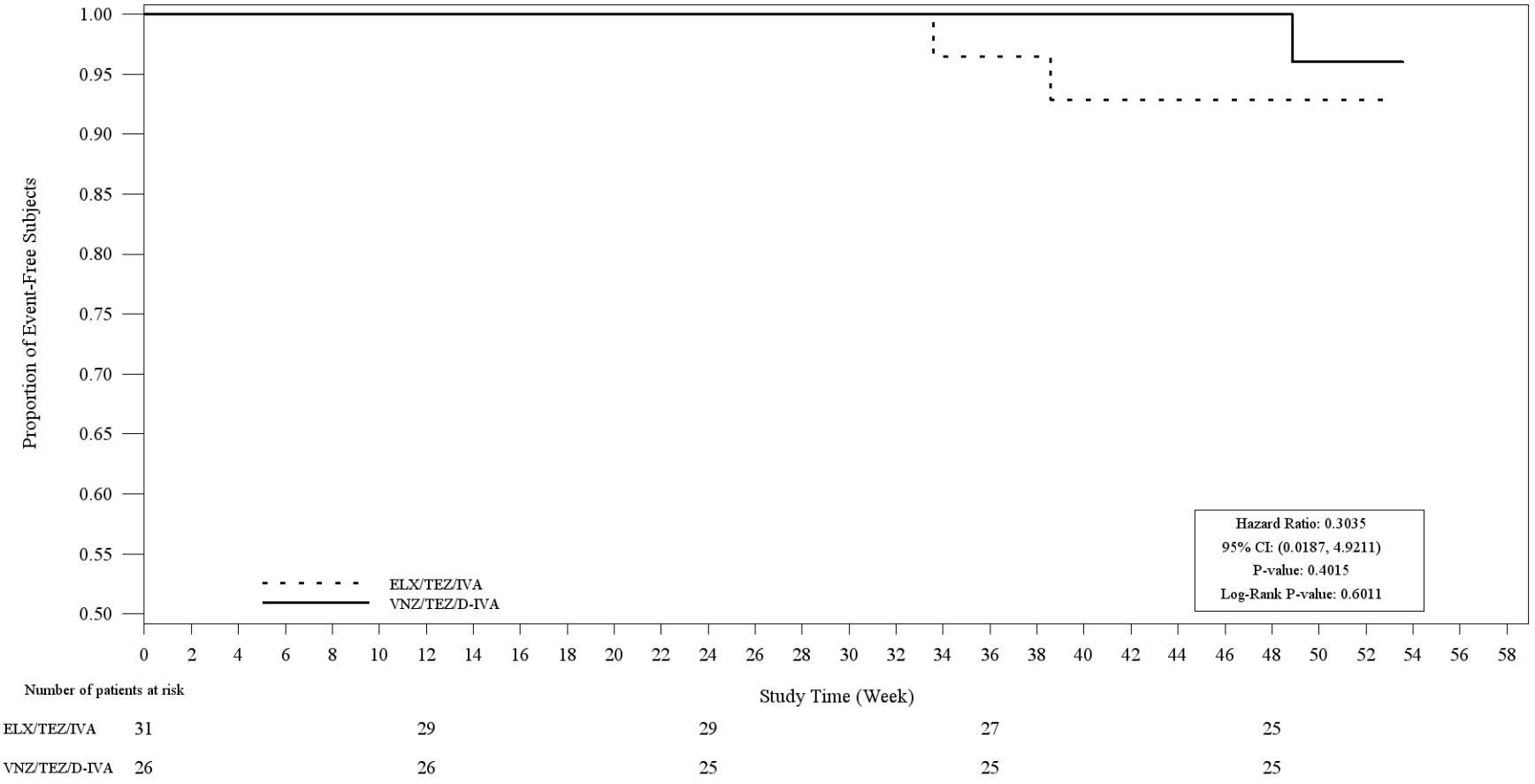
ELX/TEZ/IVA	87	83	81	75	73
VNZ/TEZ/D-IVA	92	90	87	86	86

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-iv-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening < 18 years

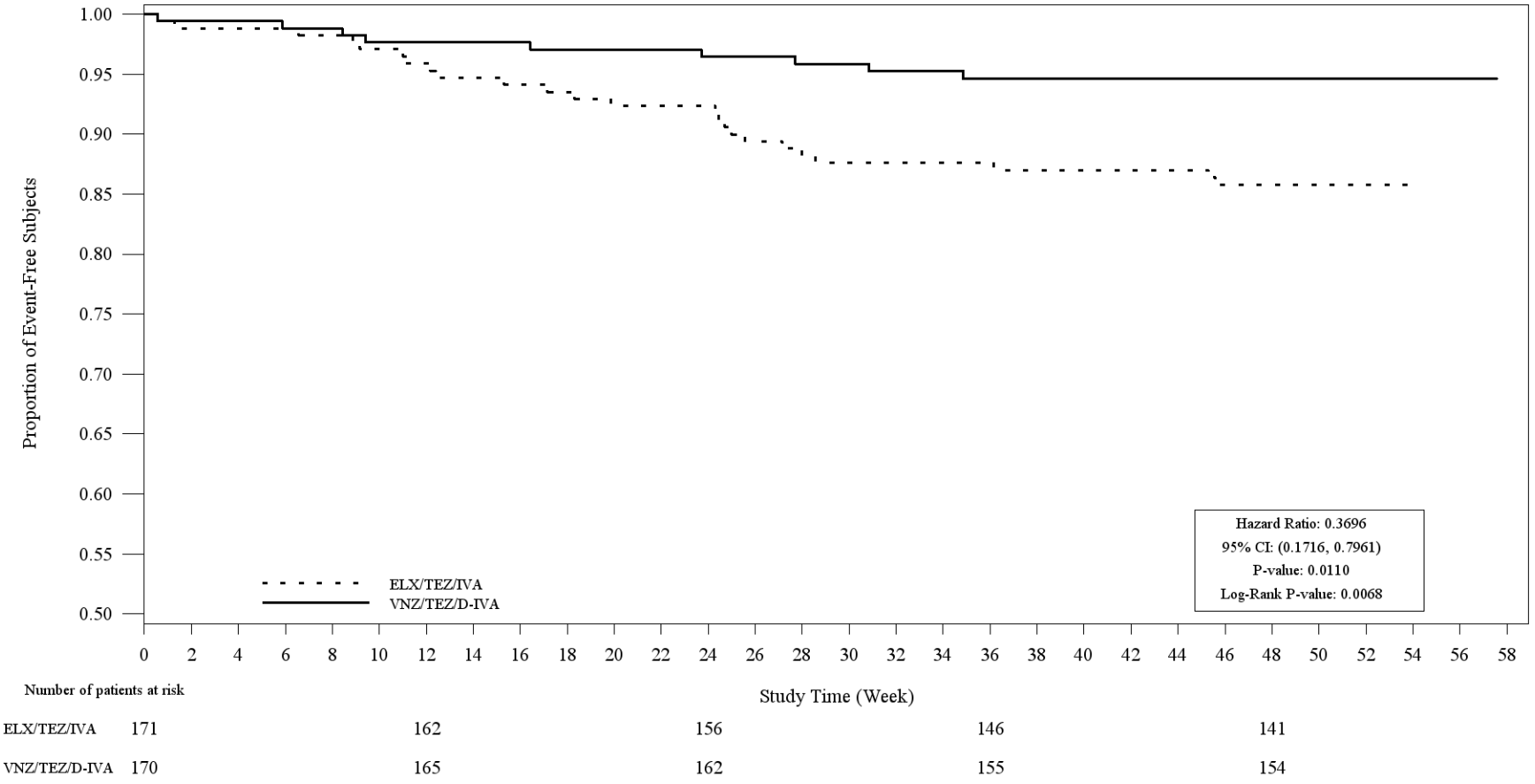


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-iv-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening ≥ 18 years



Number of patients at risk

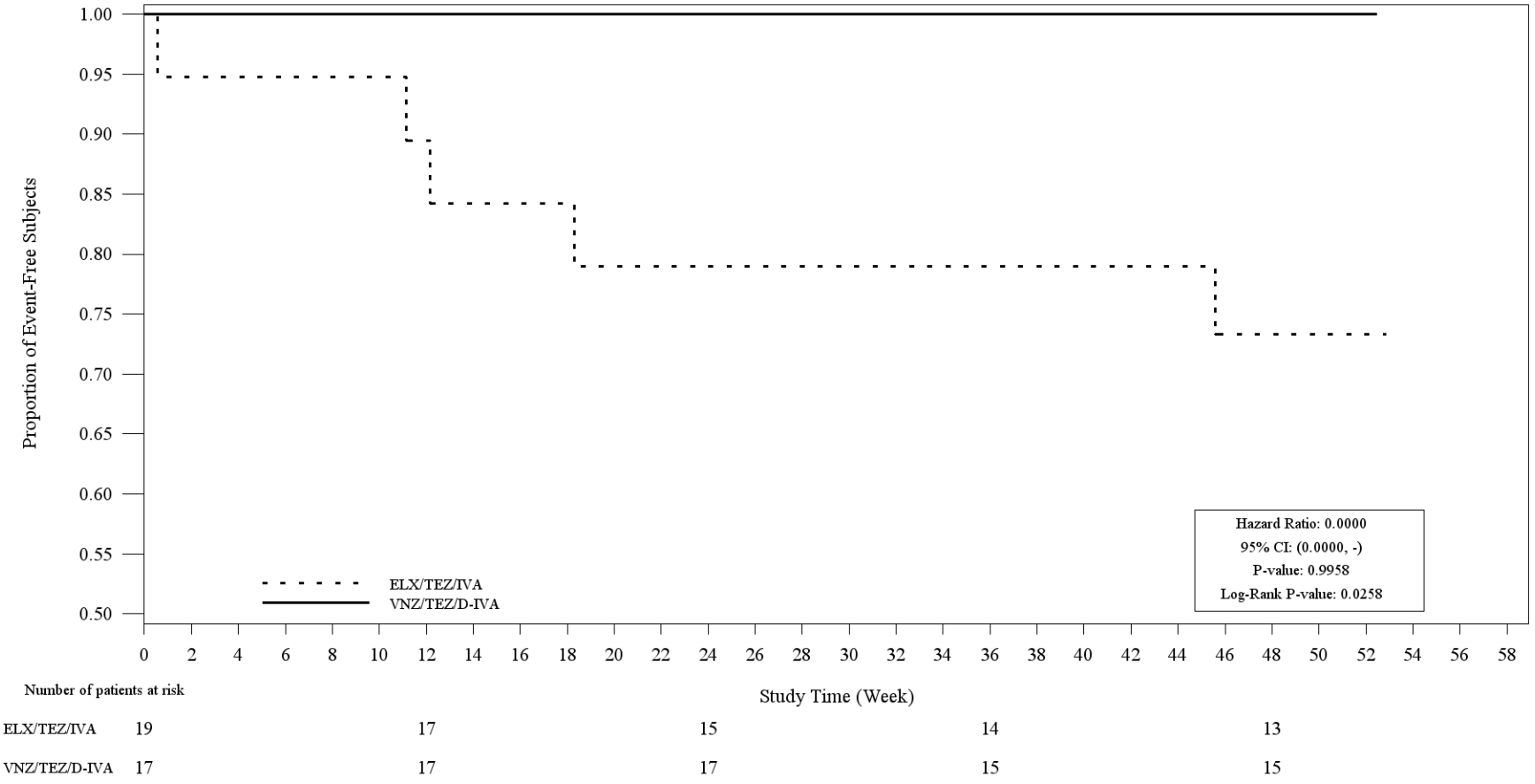
ELX/TEZ/IVA	171	162	156	146	141
VNZ/TEZ/D-IVA	170	165	162	155	154

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-iv-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline <30 mmol/L



Number of patients at risk

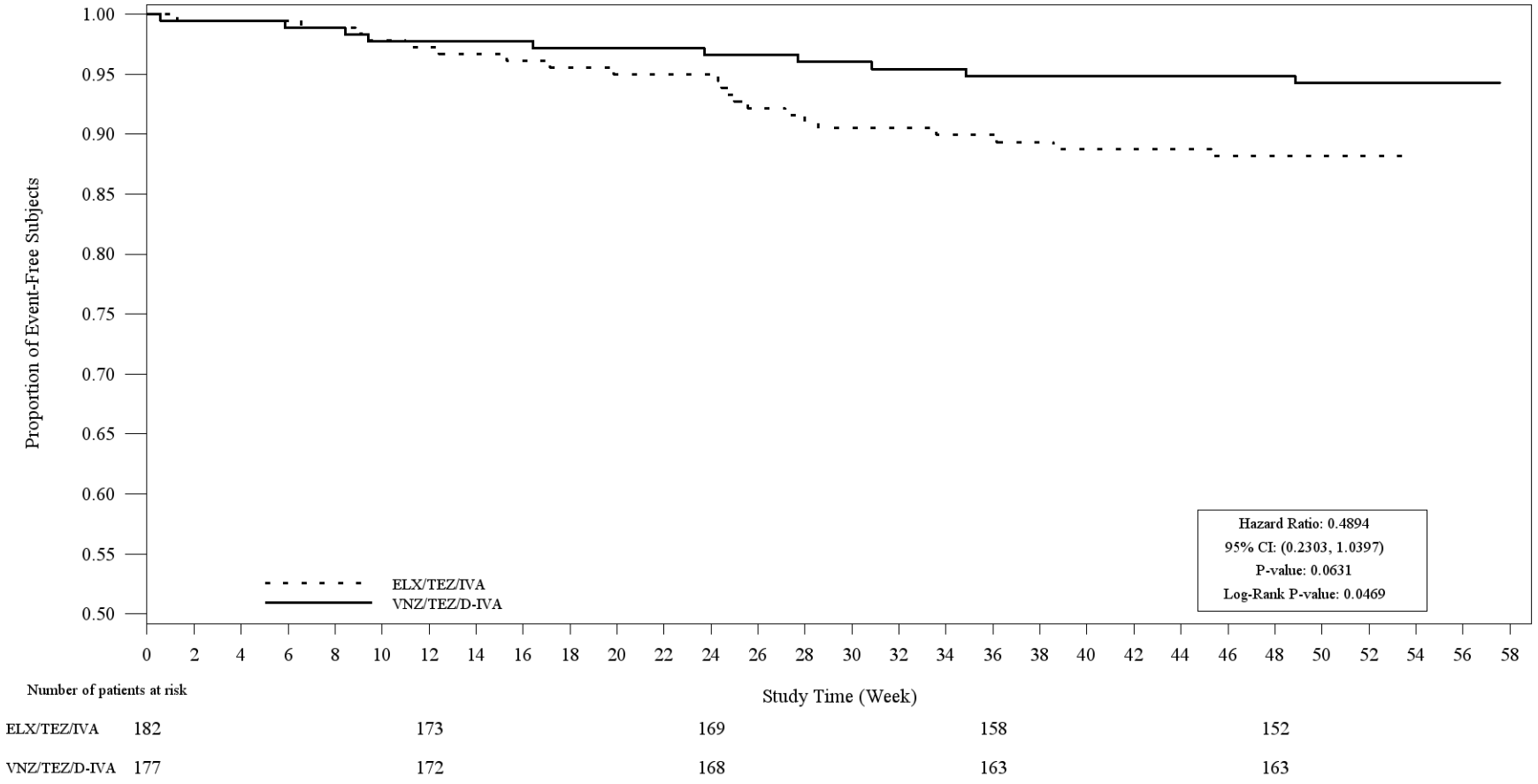
ELX/TEZ/IVA	19	17	15	14	13
VNZ/TEZ/D-IVA	17	17	17	15	15

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-iv-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline ≥30 mmol/L



Number of patients at risk

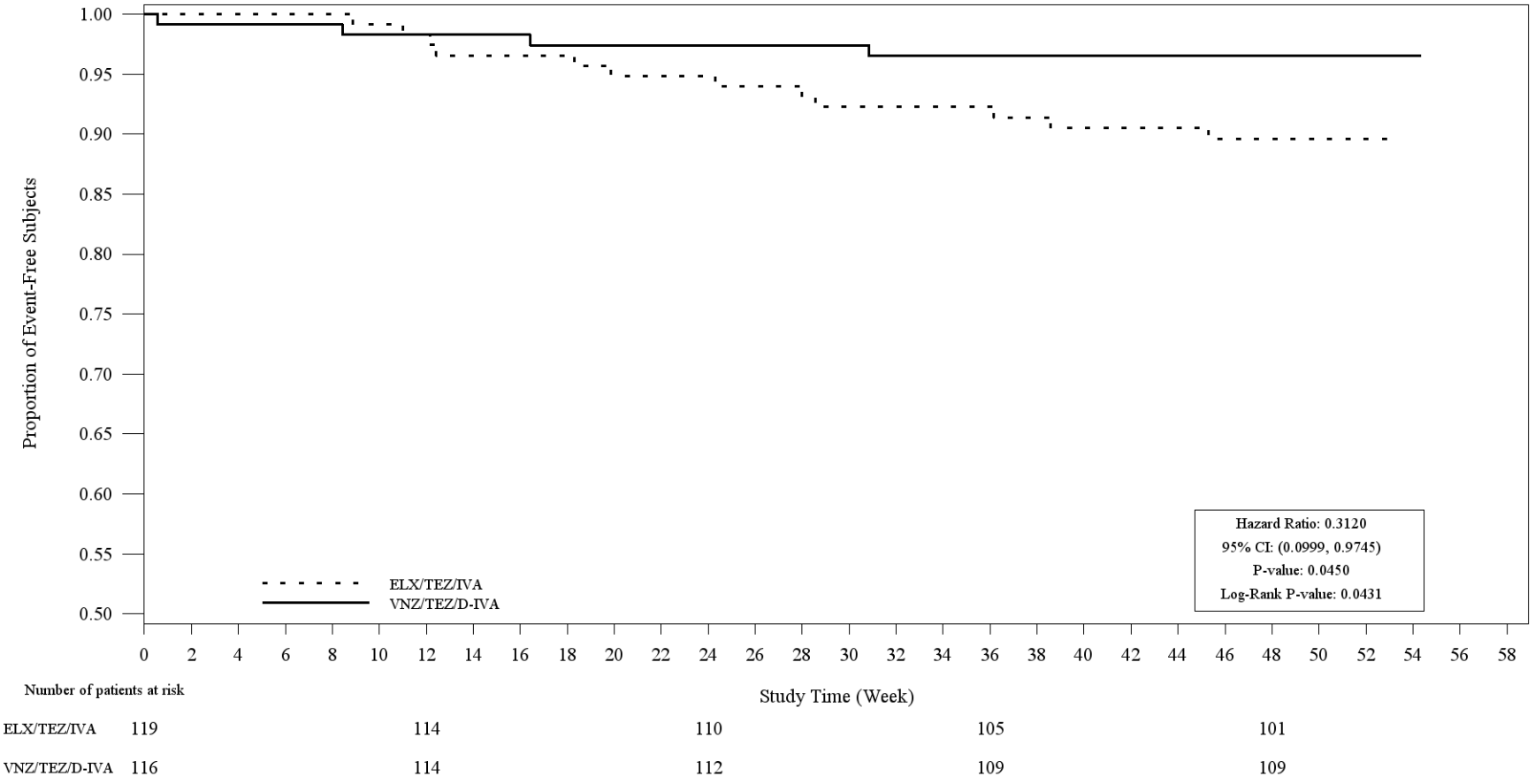
ELX/TEZ/IVA	182	173	169	158	152
VNZ/TEZ/D-IVA	177	172	168	163	163

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-iv-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Male

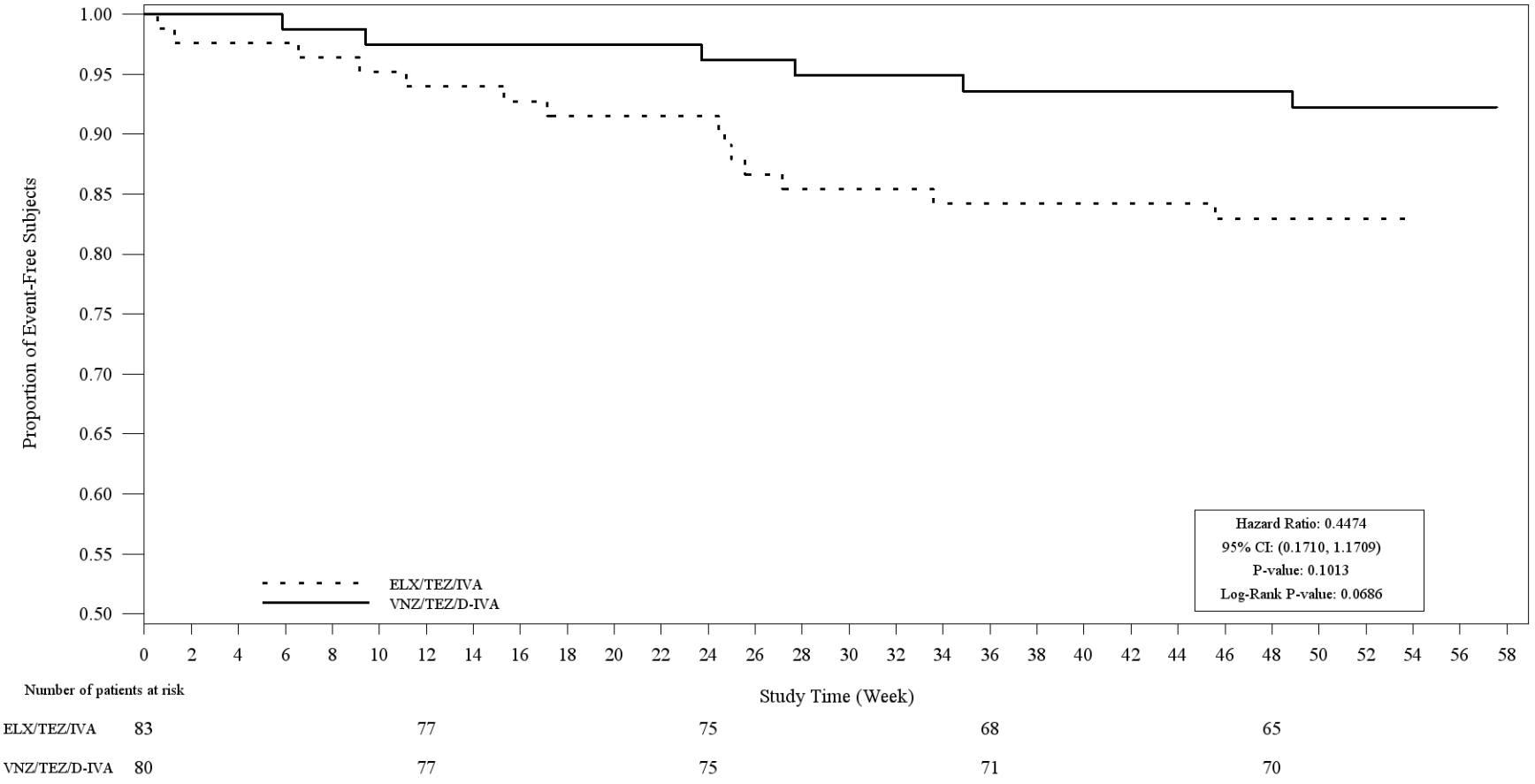


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-iv-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Female



Number of patients at risk

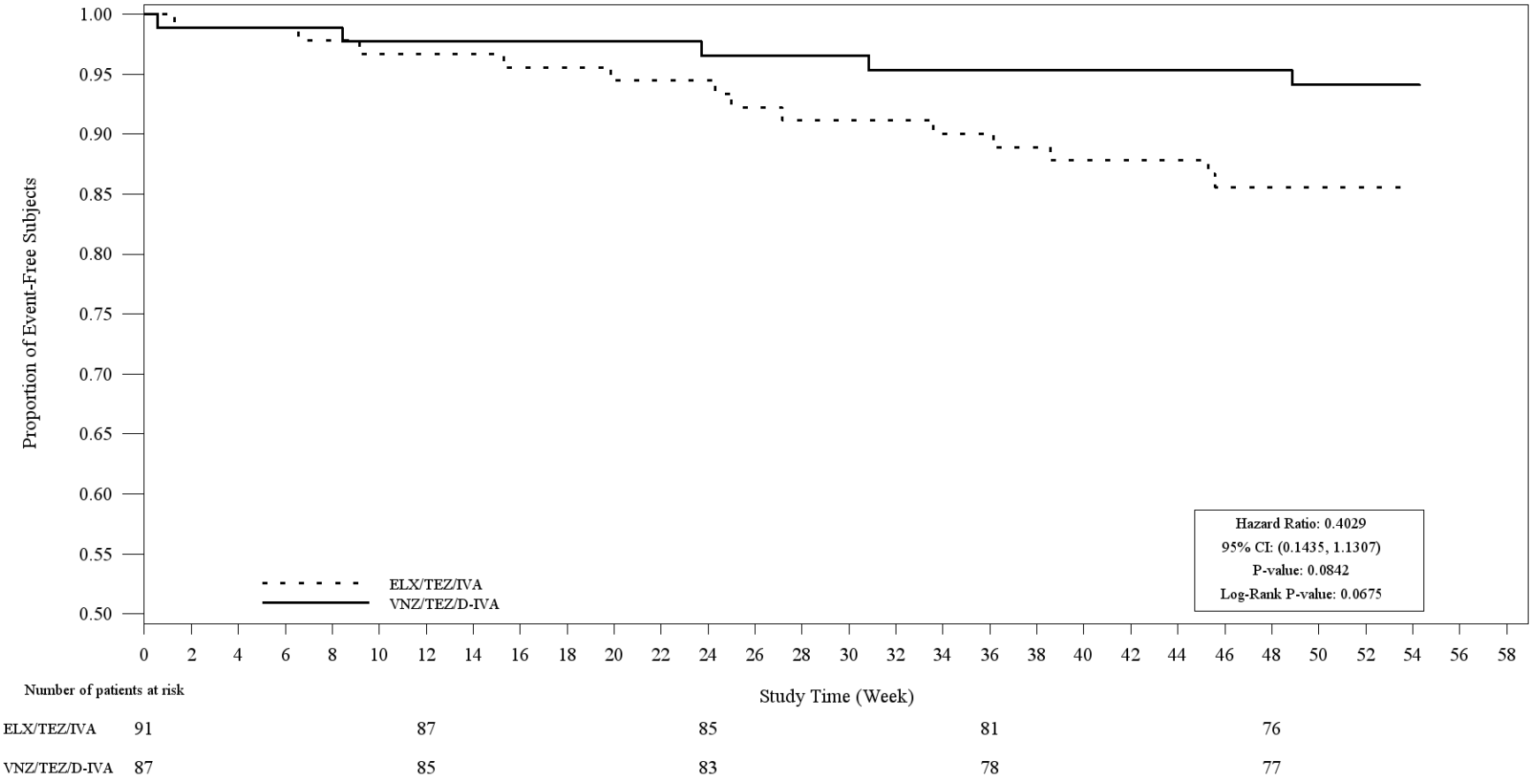
ELX/TEZ/IVA	83	77	75	68	65
VNZ/TEZ/D-IVA	80	77	75	71	70

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-iv-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = North America

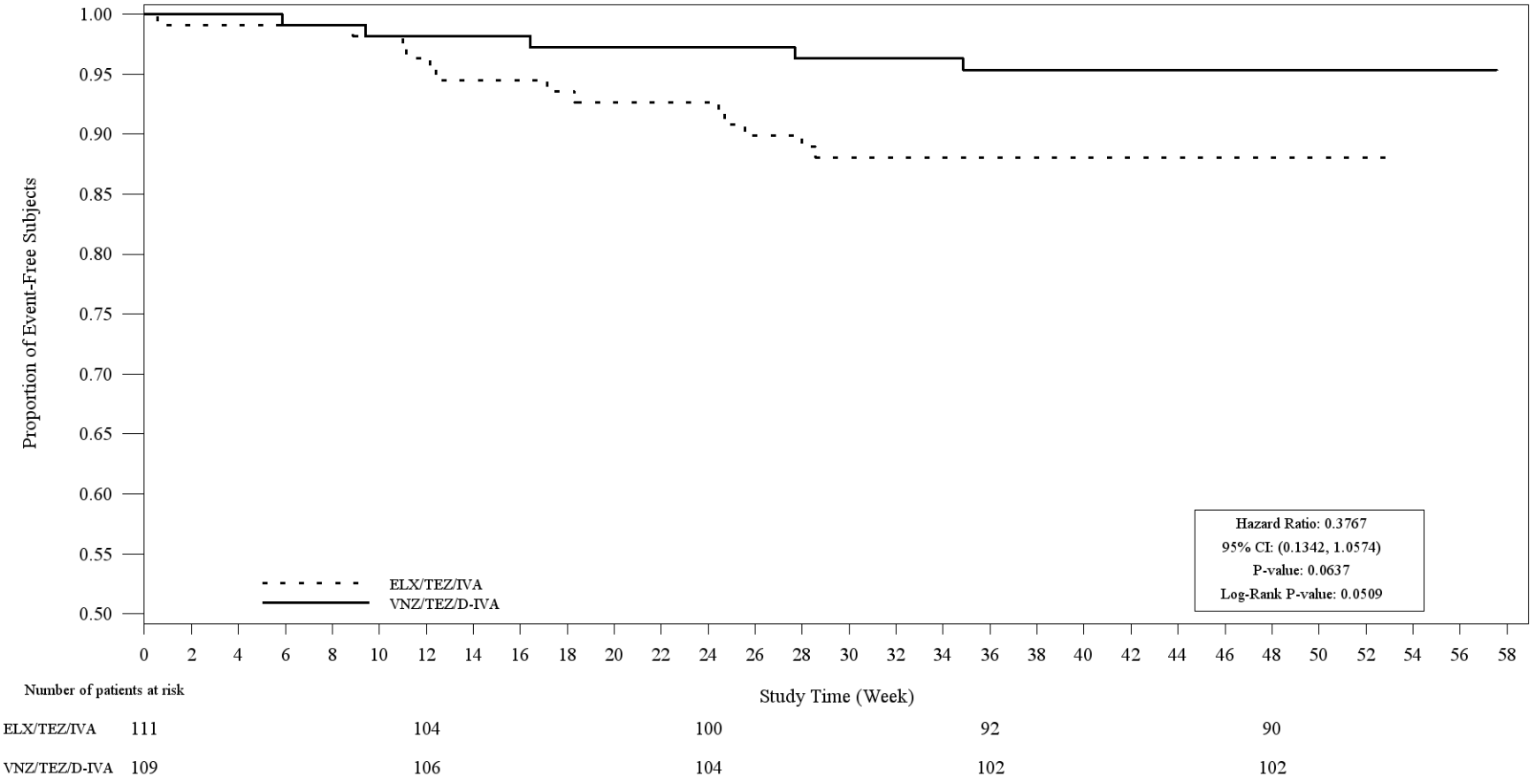


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-iv-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = Rest of the World

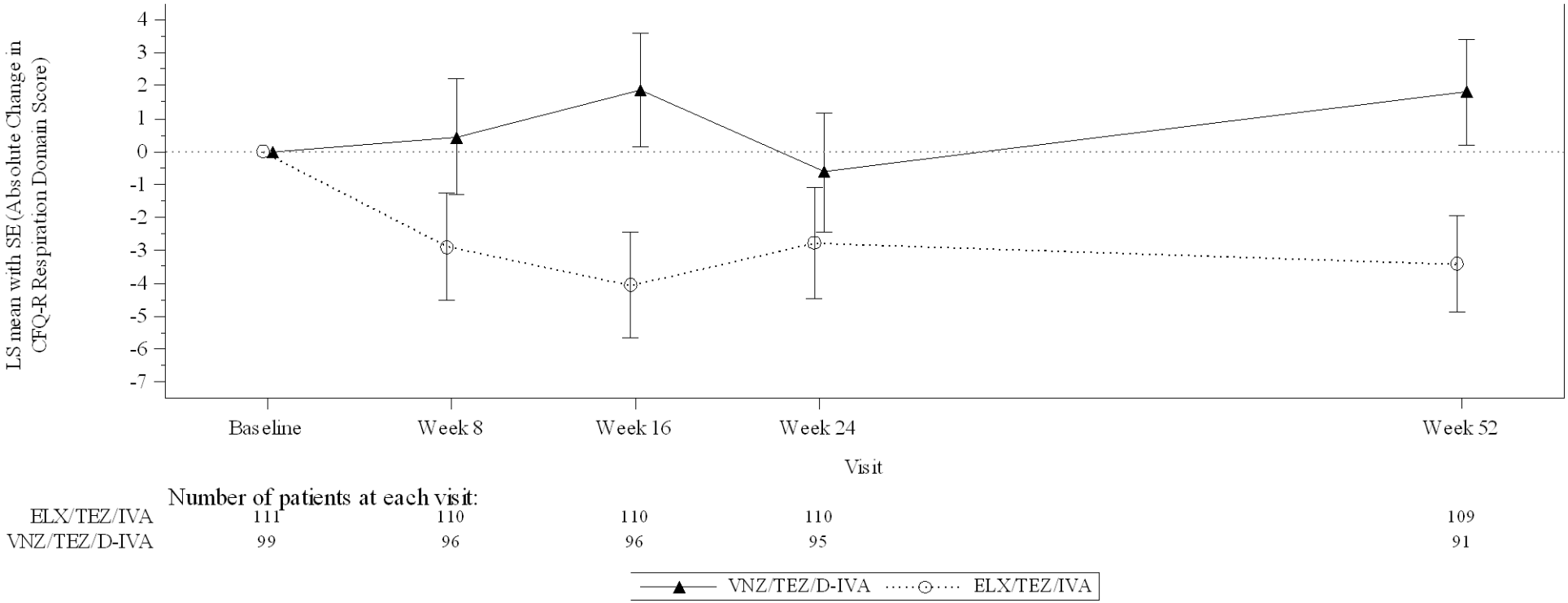


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-ce-pe-iv-km-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
ppFEV$_1$ at baseline <70 %

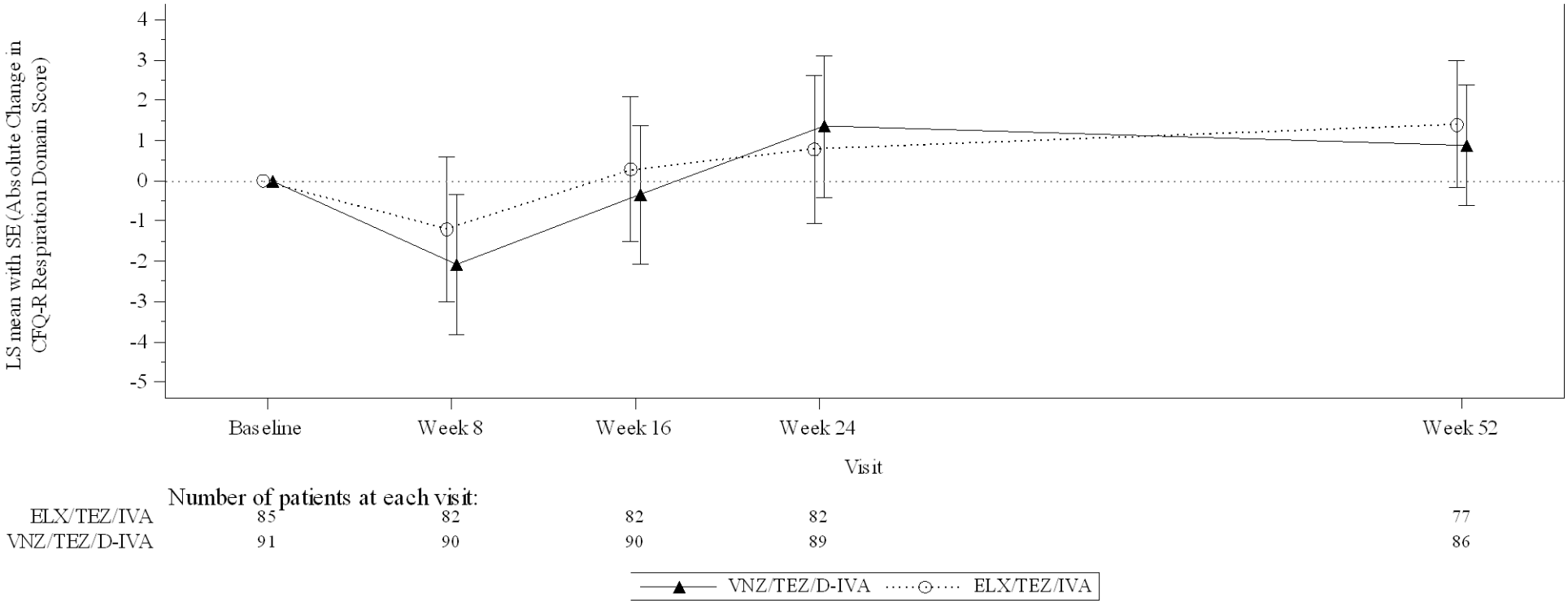


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
ppFEV$_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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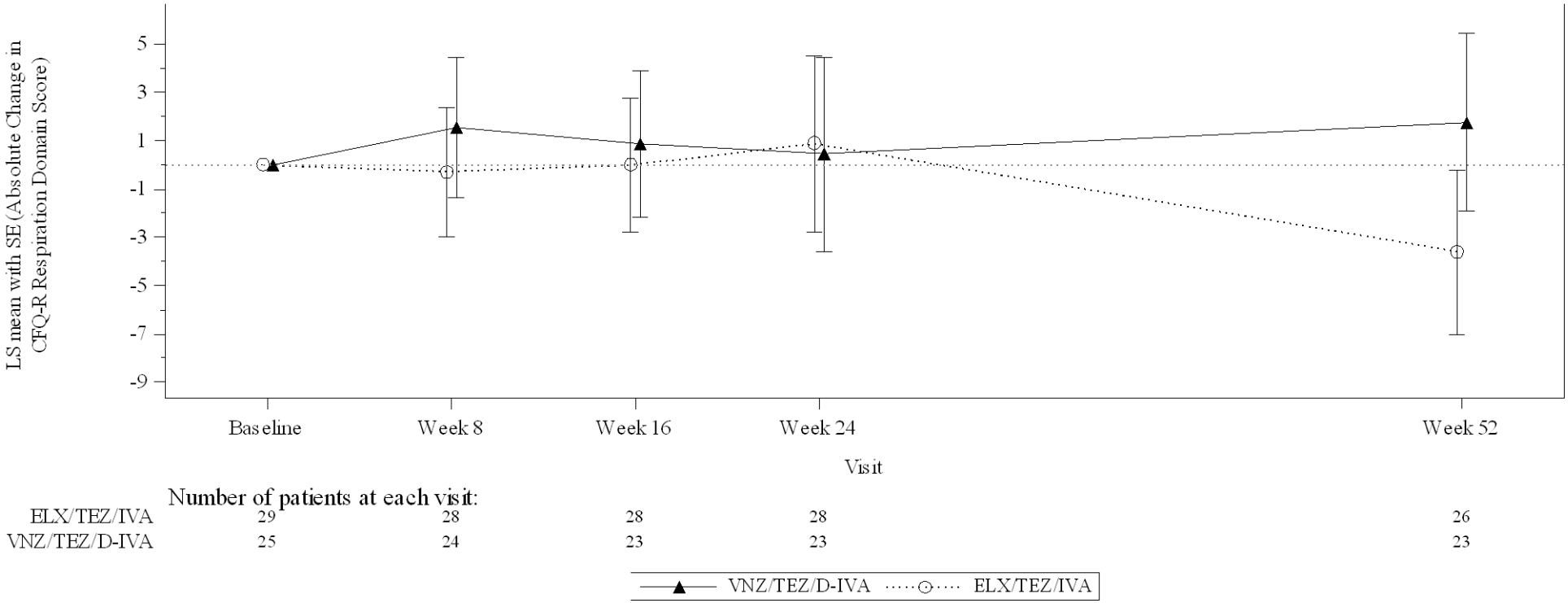
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Age at screening <18 years



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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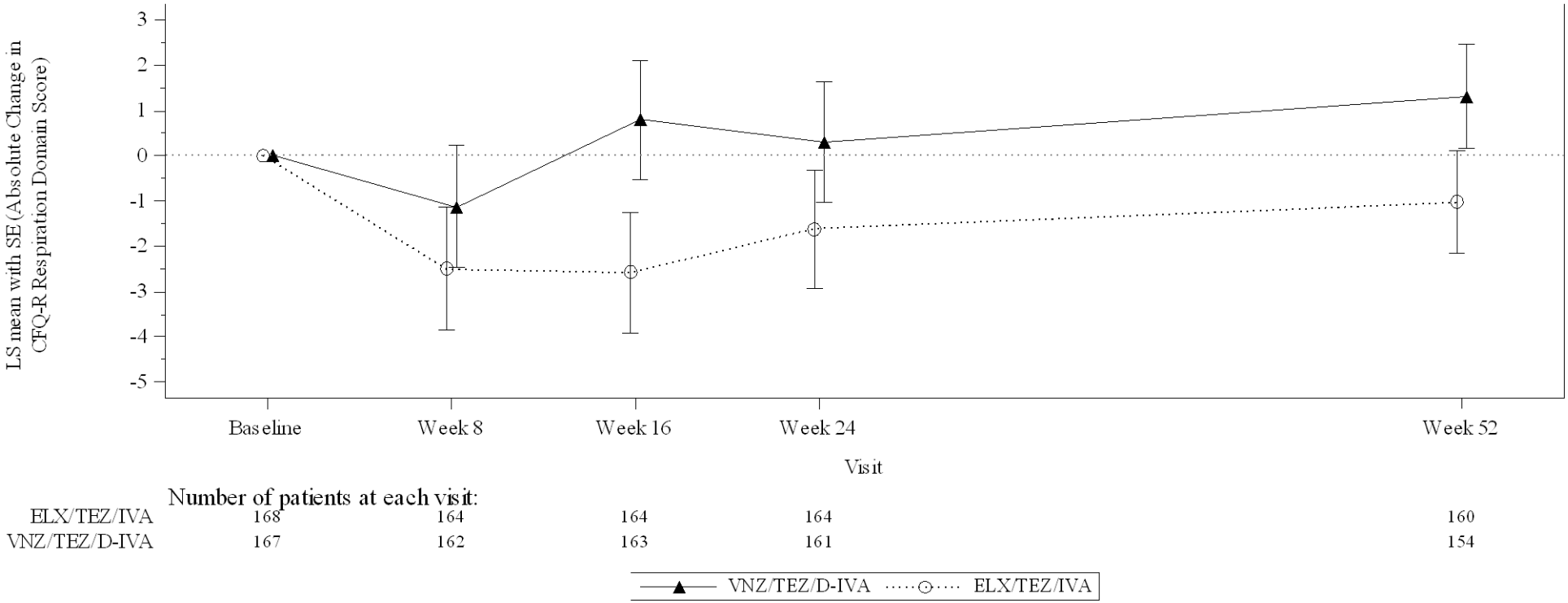
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Age at screening ≥18 years

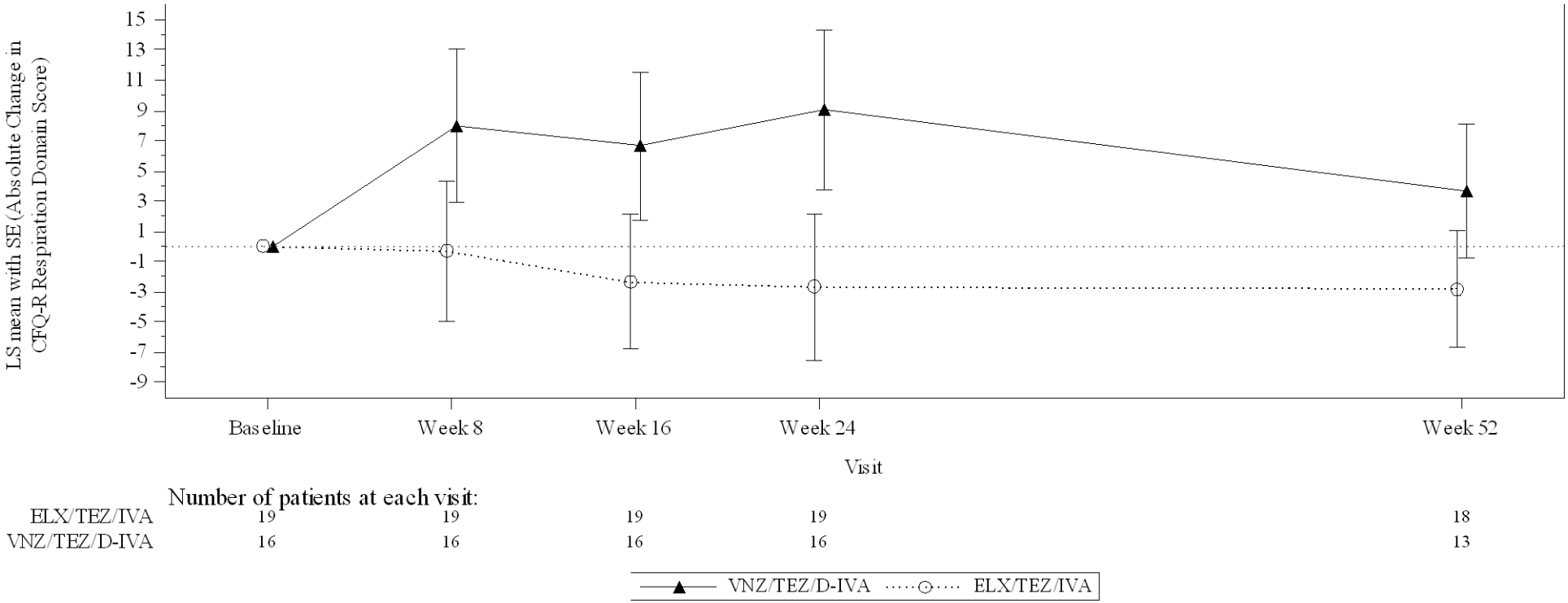


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
SwCl at baseline <30 mmol/L

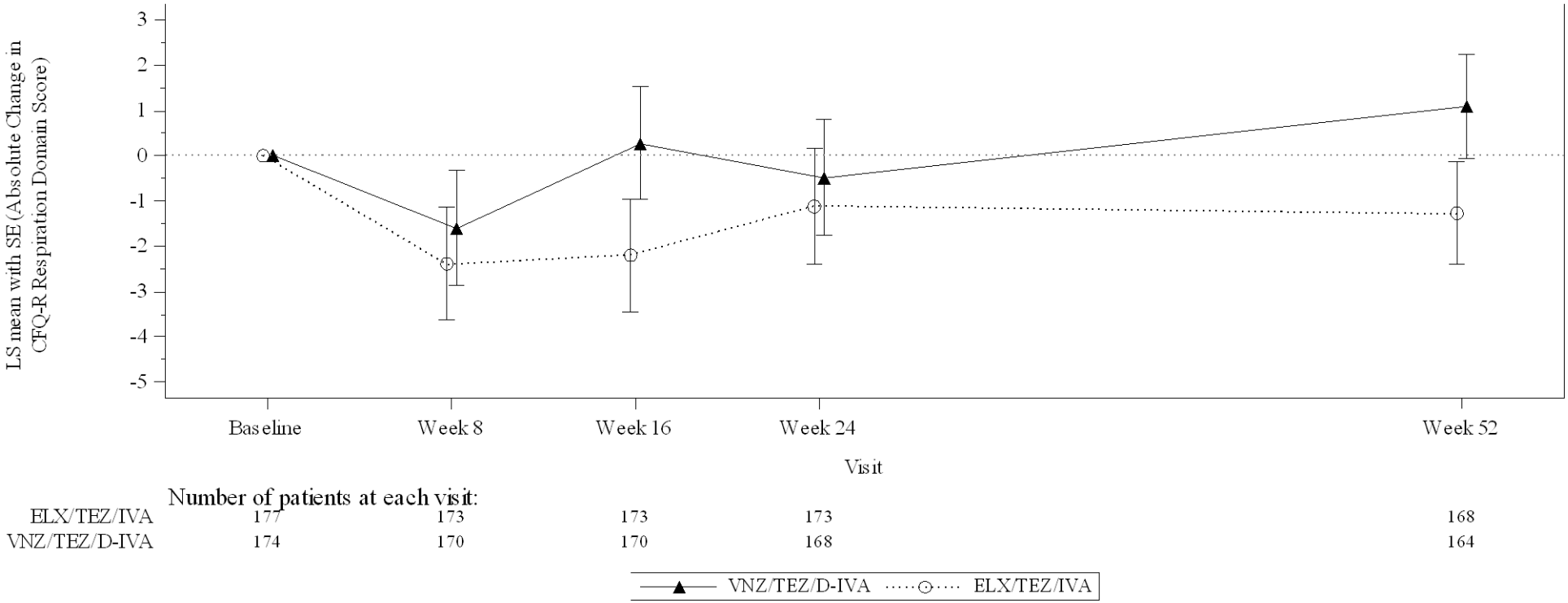


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
SwCl at baseline ≥30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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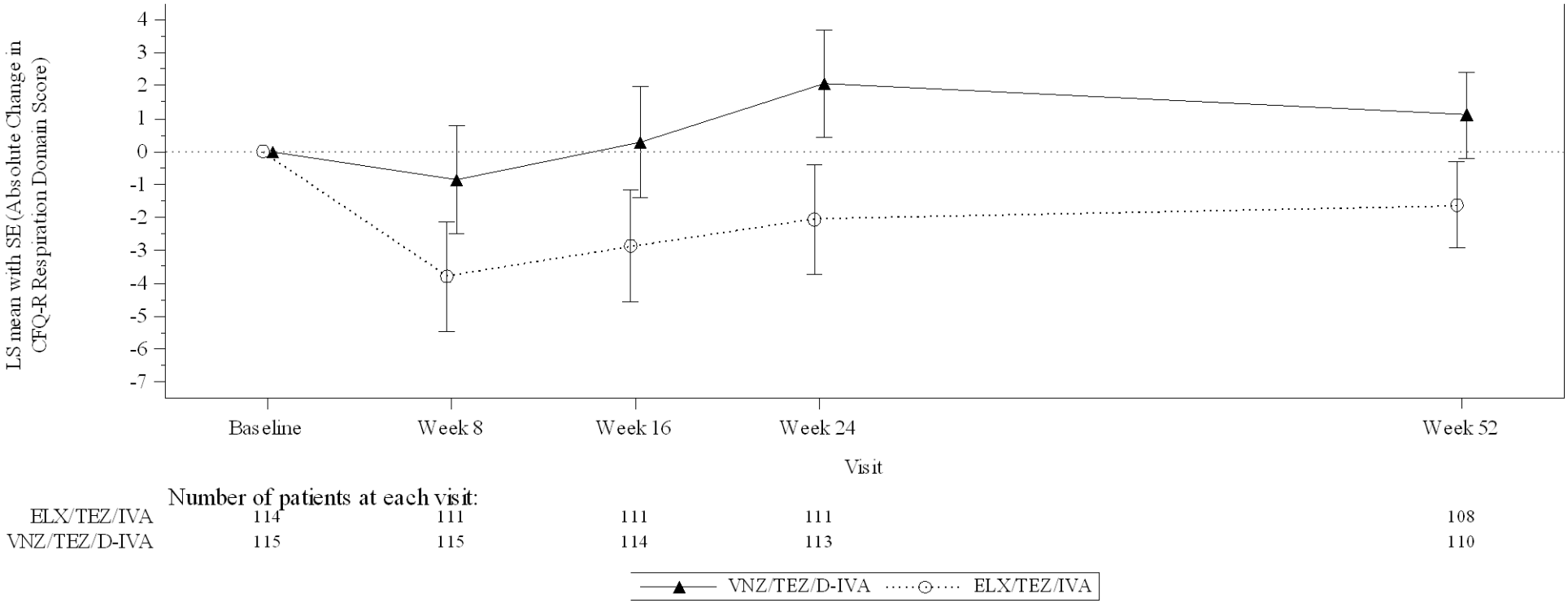
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Sex = Male

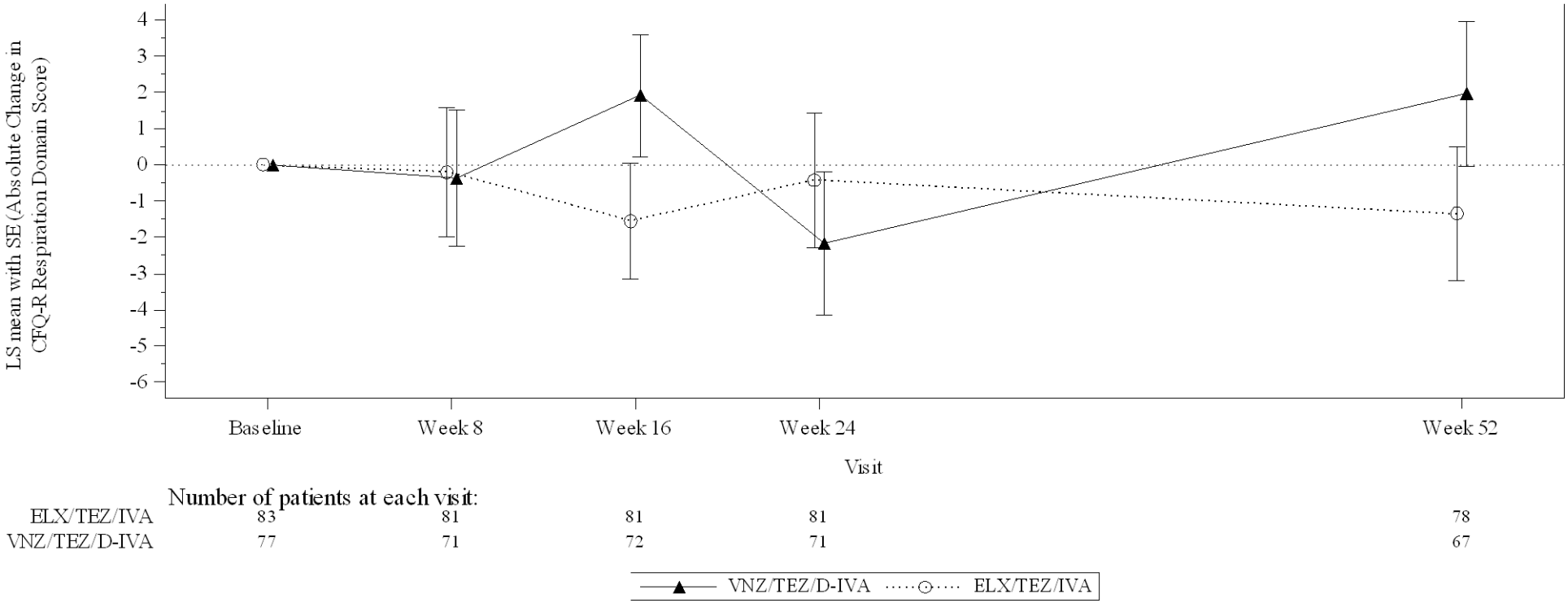


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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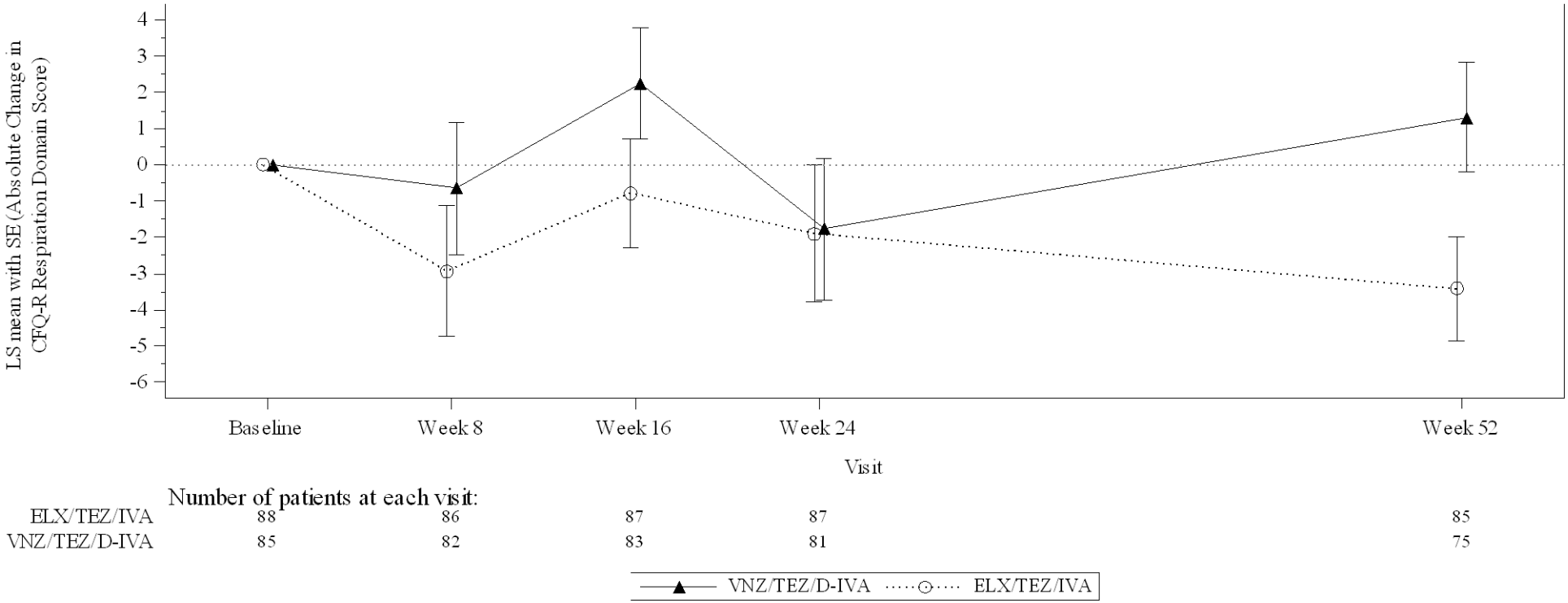
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Region = North America



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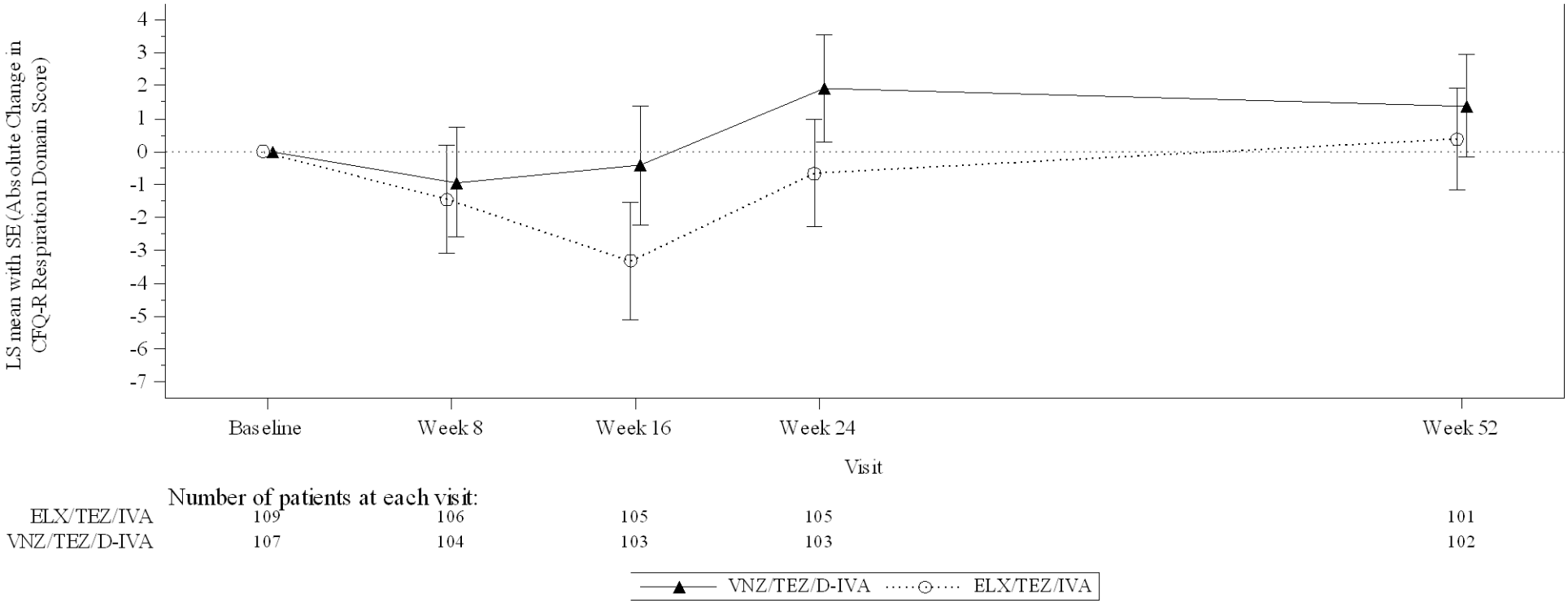
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Region = Rest of World



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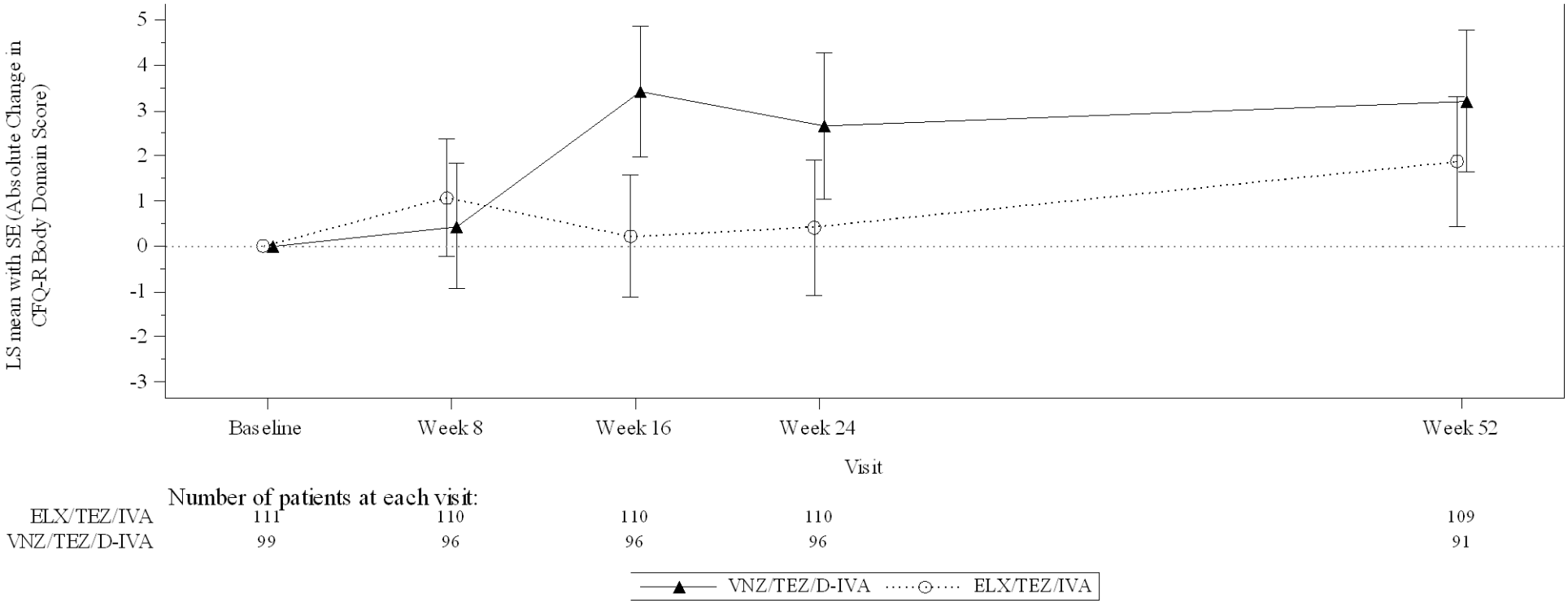
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
ppFEV$_1$ at baseline <70 %



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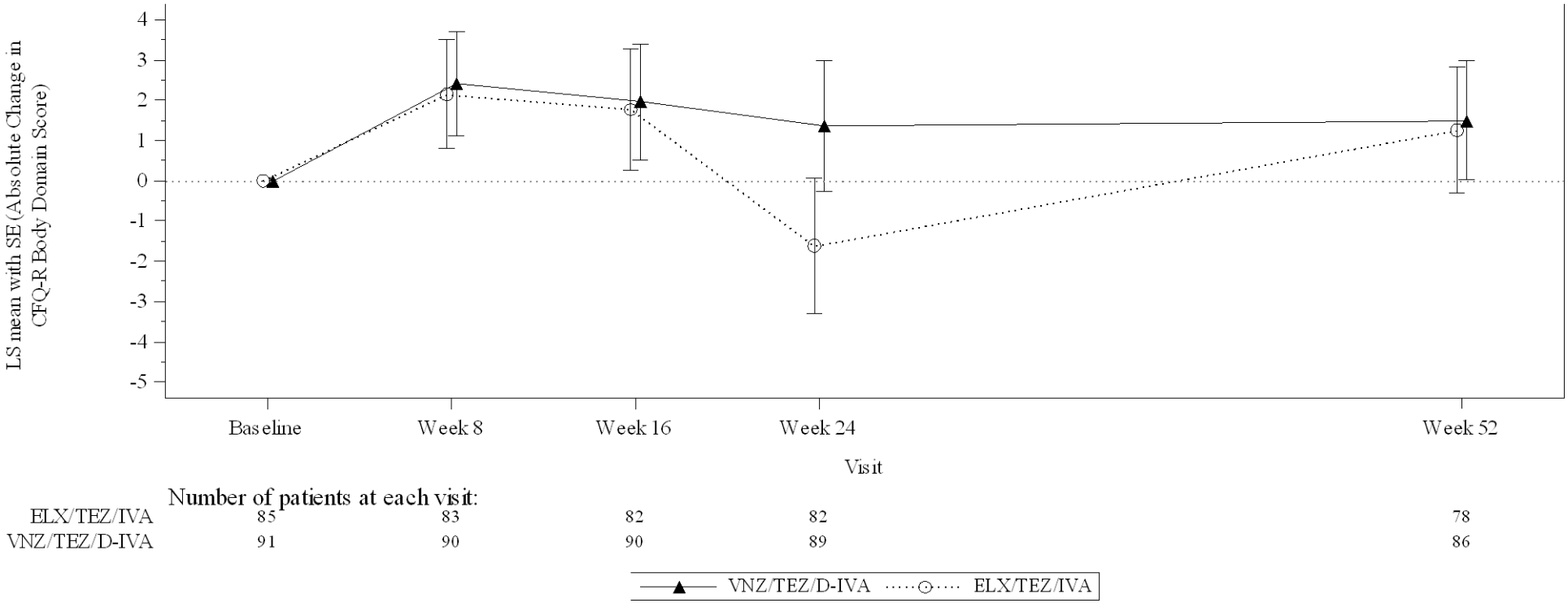
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
ppFEV$_1$ at baseline ≥70 %



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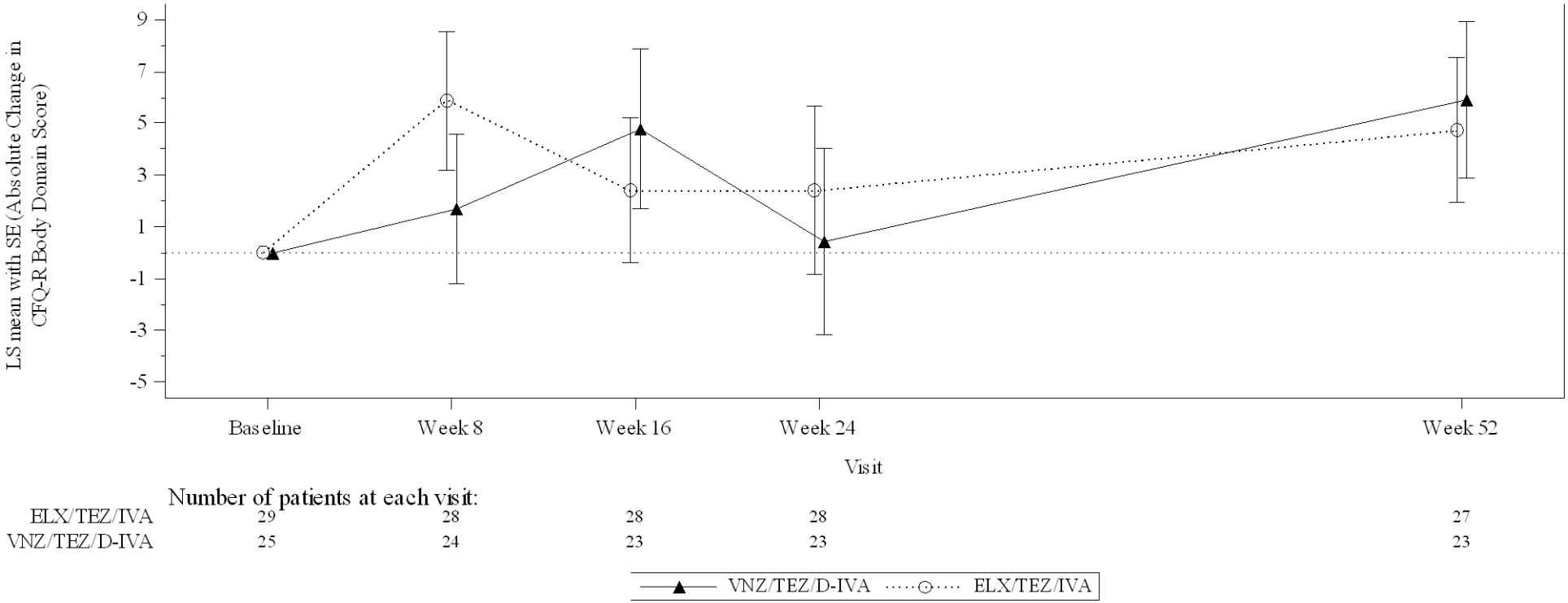
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years



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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

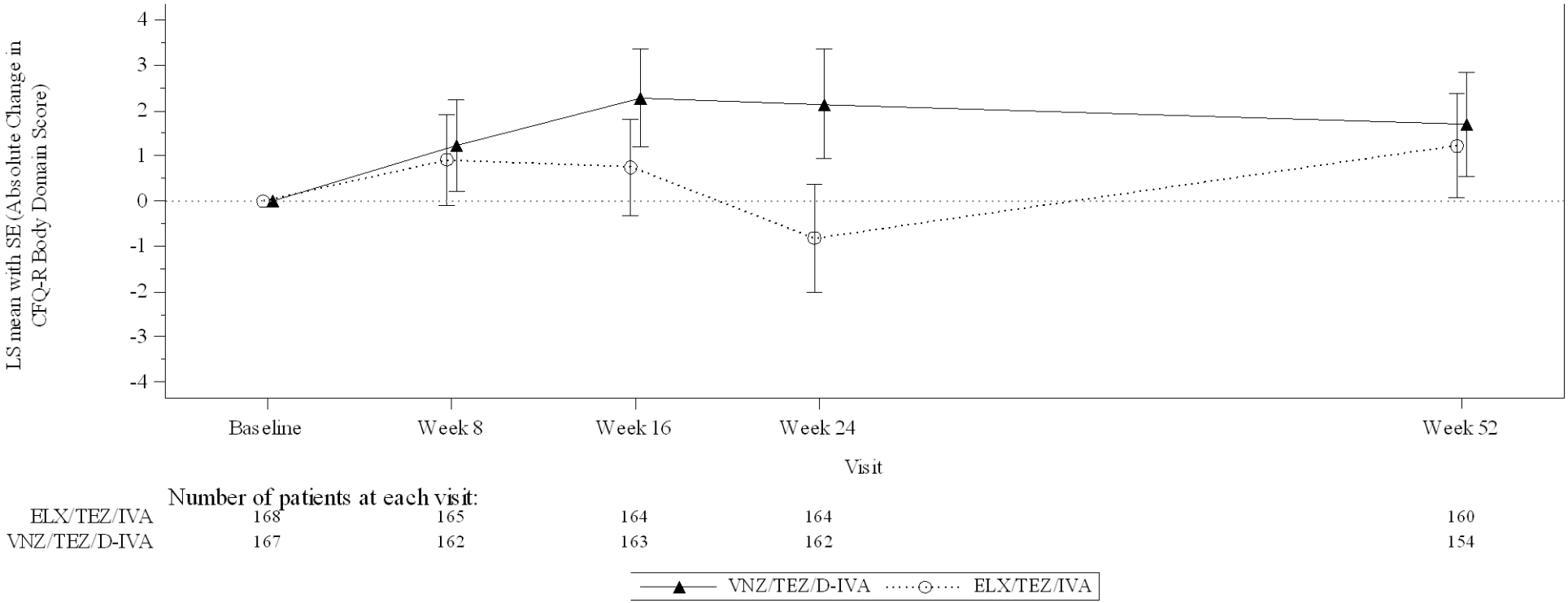

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Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

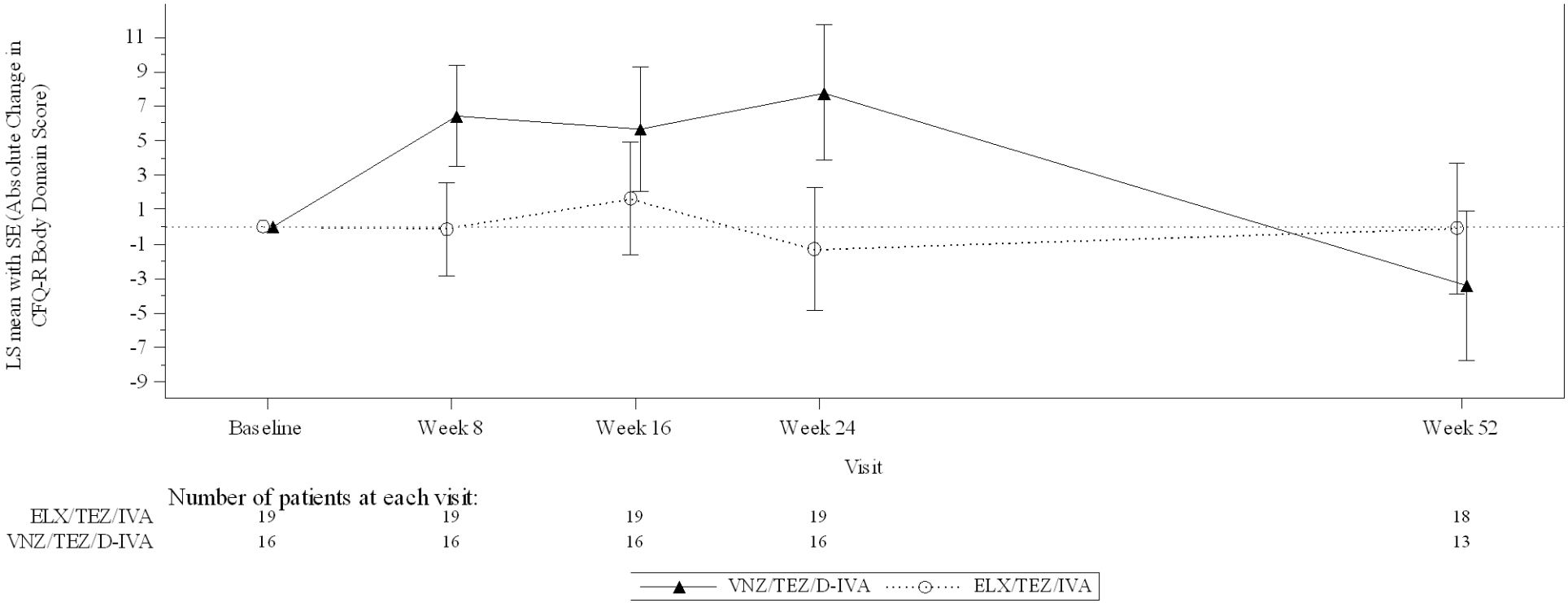

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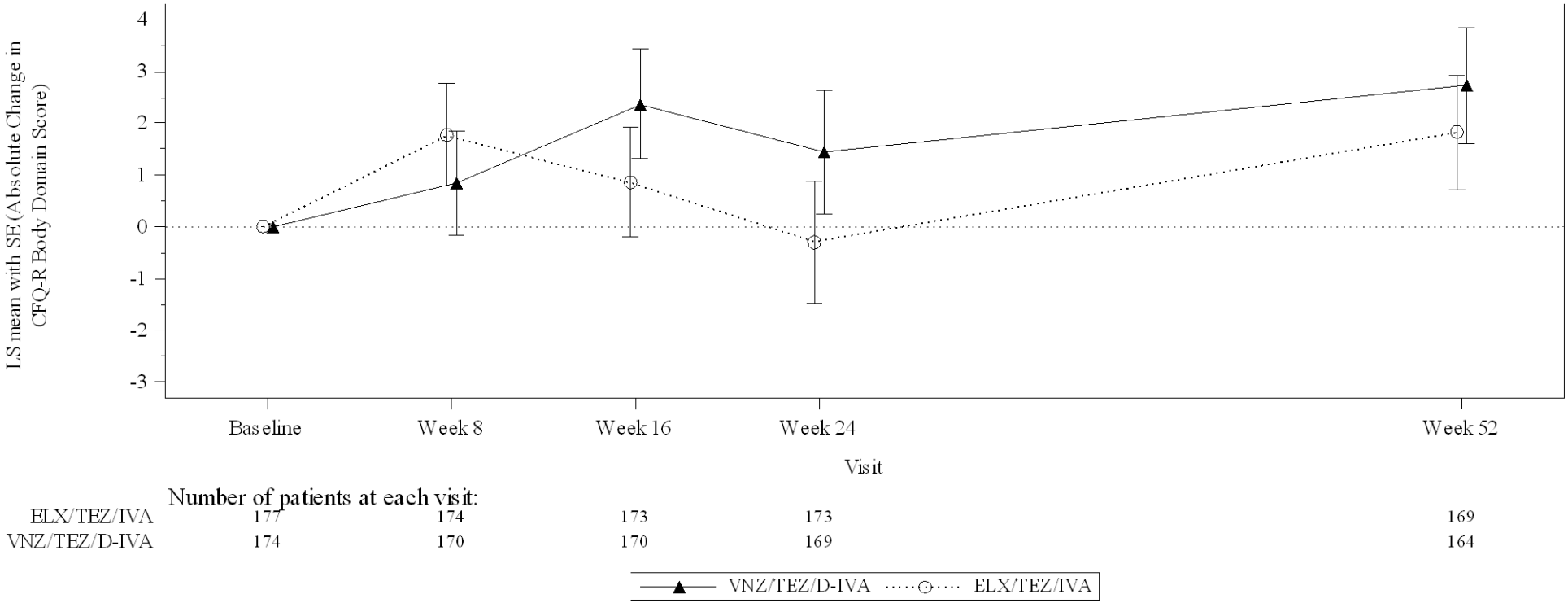
Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L



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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

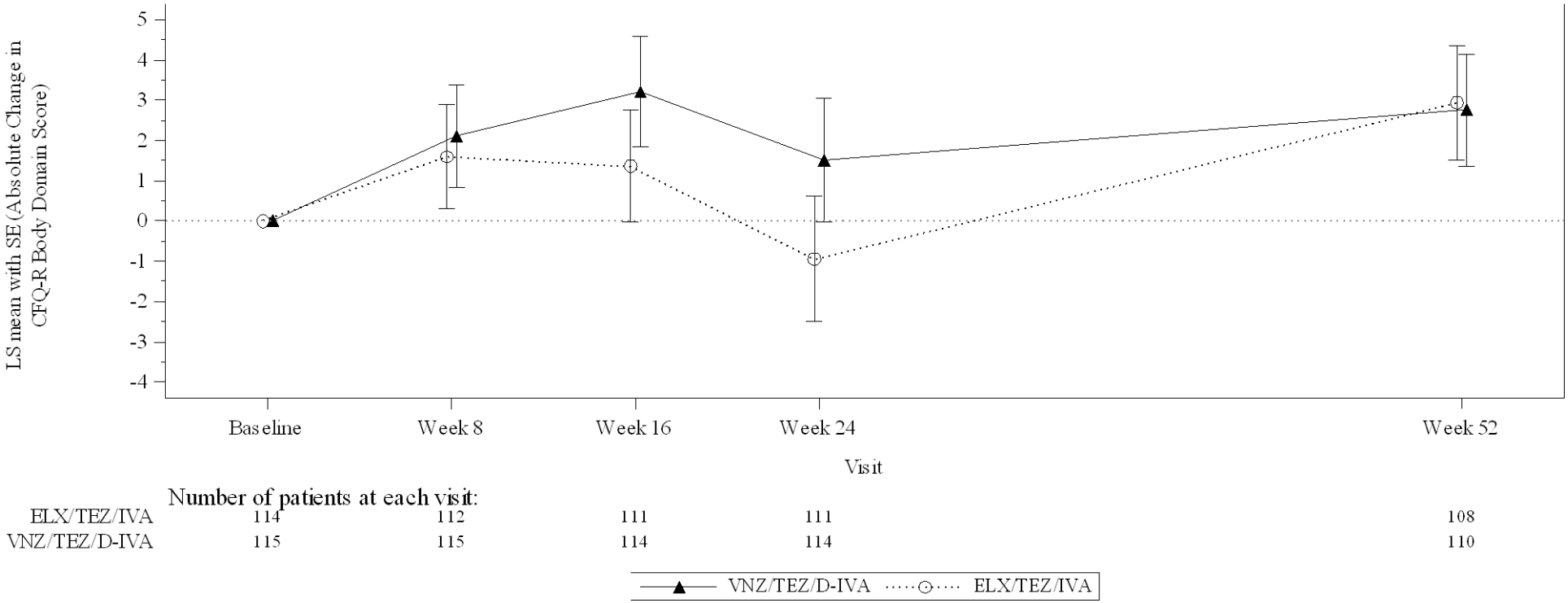

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Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

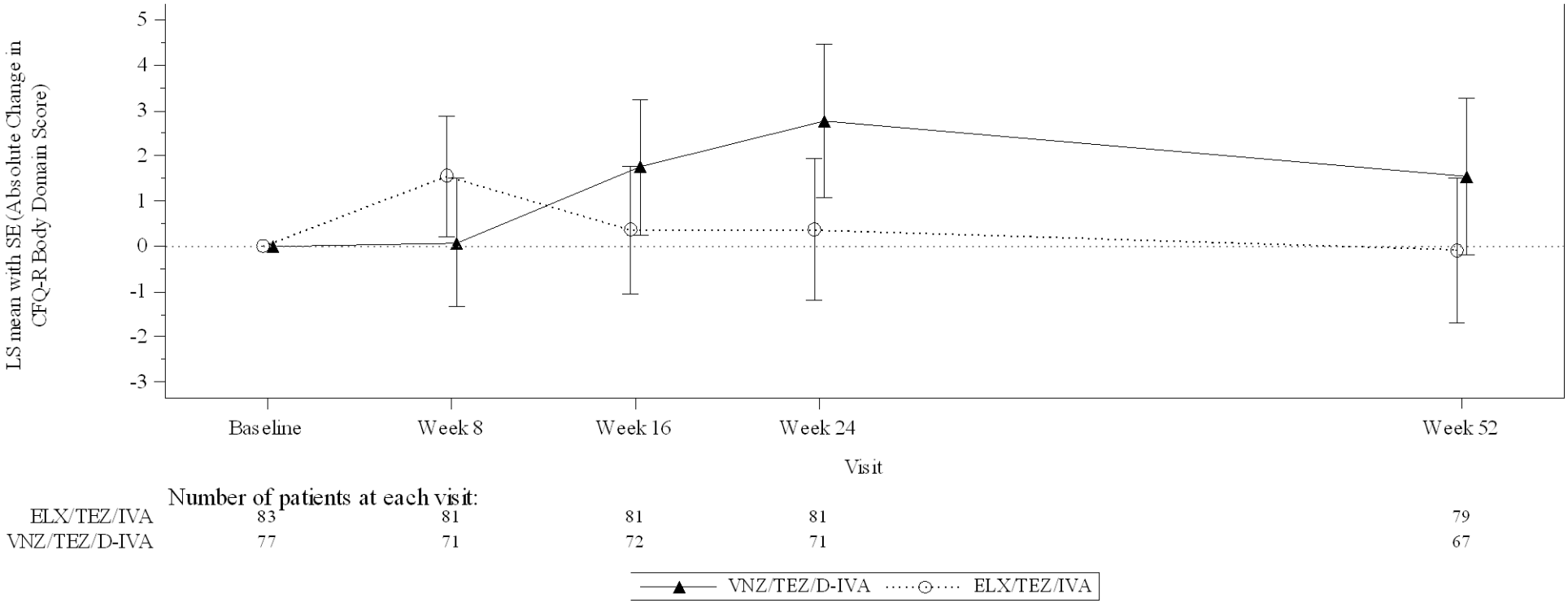

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Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

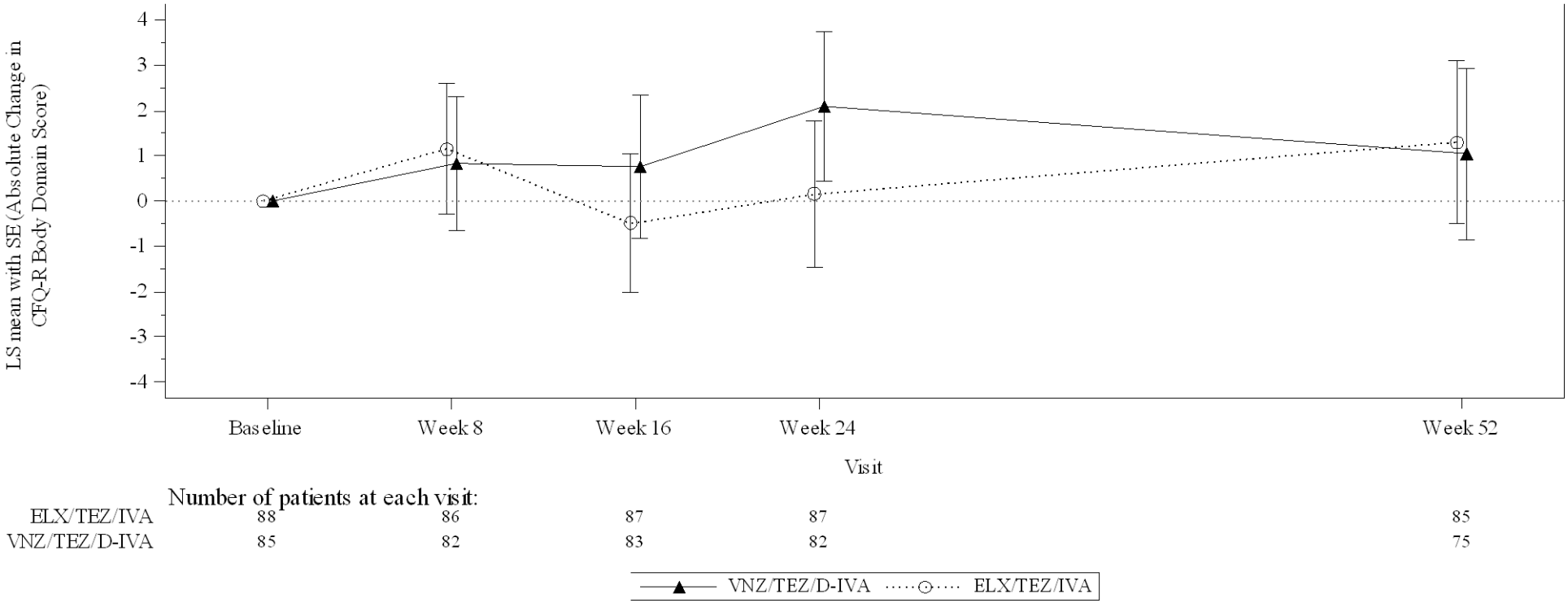

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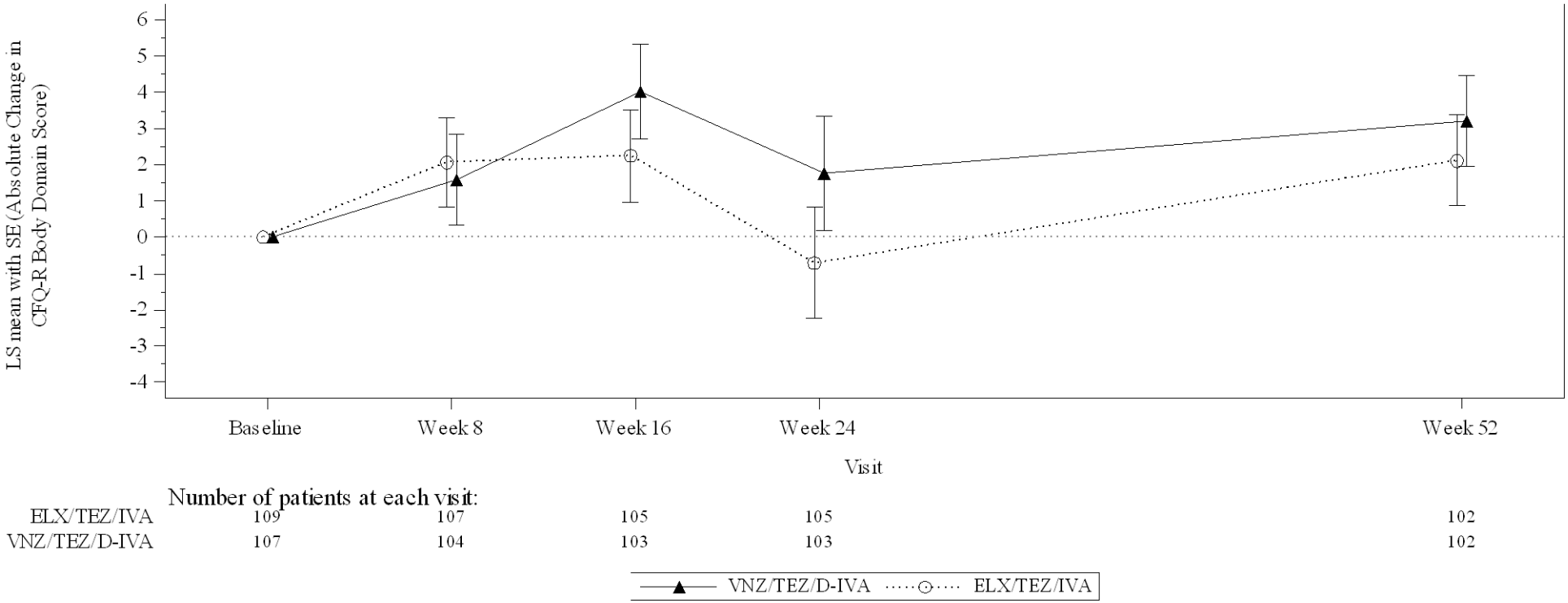
Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World



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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
ppFEV$_1$ at baseline <70 %

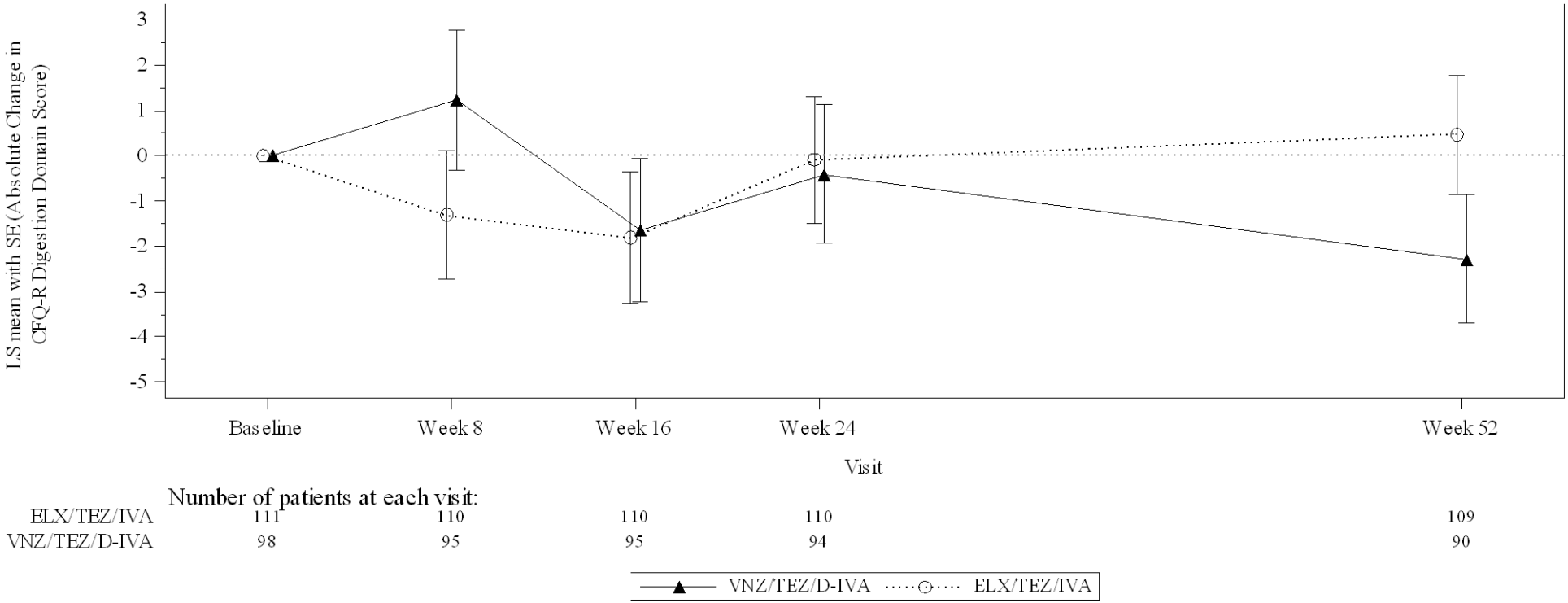

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Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
ppFEV$_1$ at baseline ≥70 %

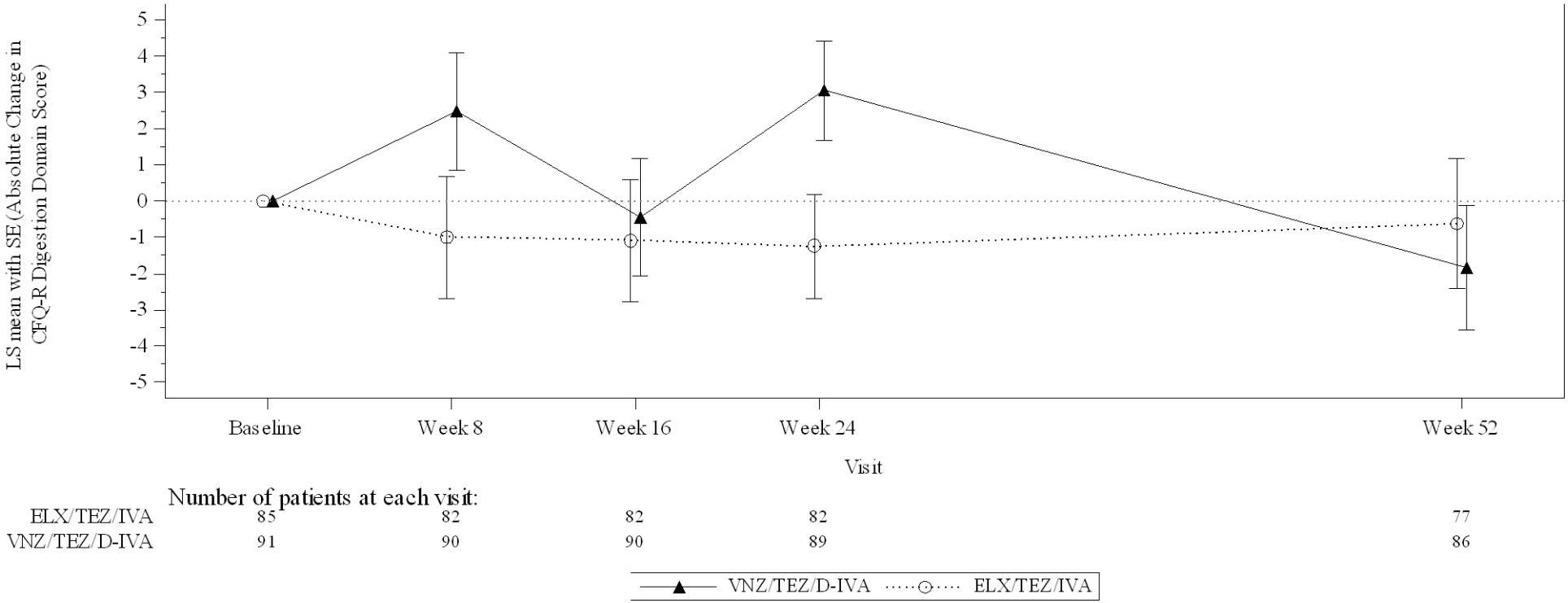

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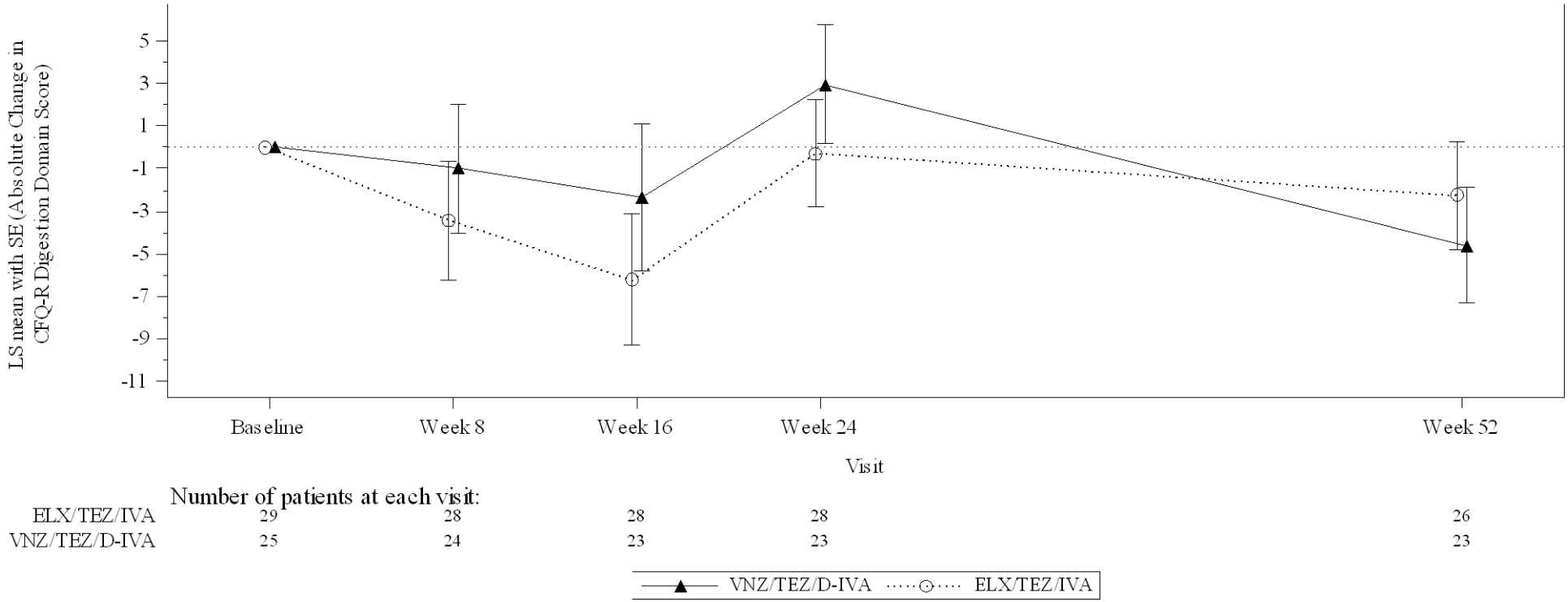
Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years



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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

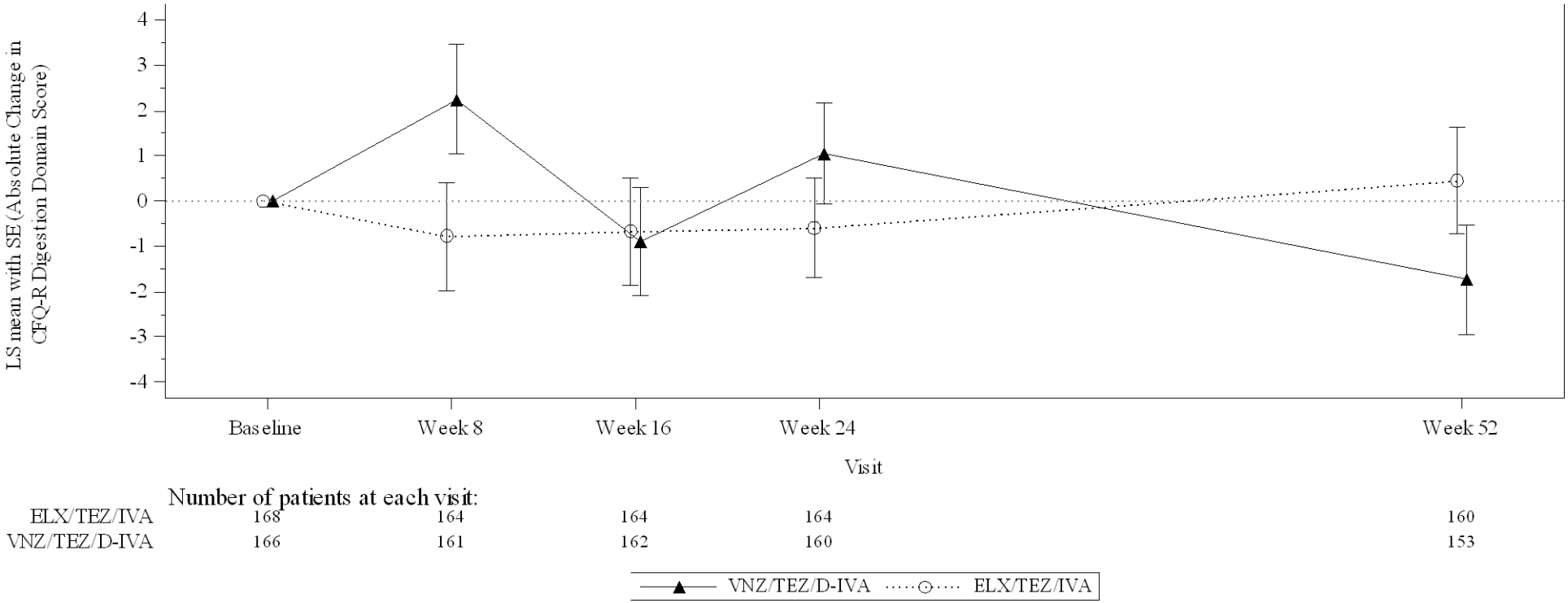

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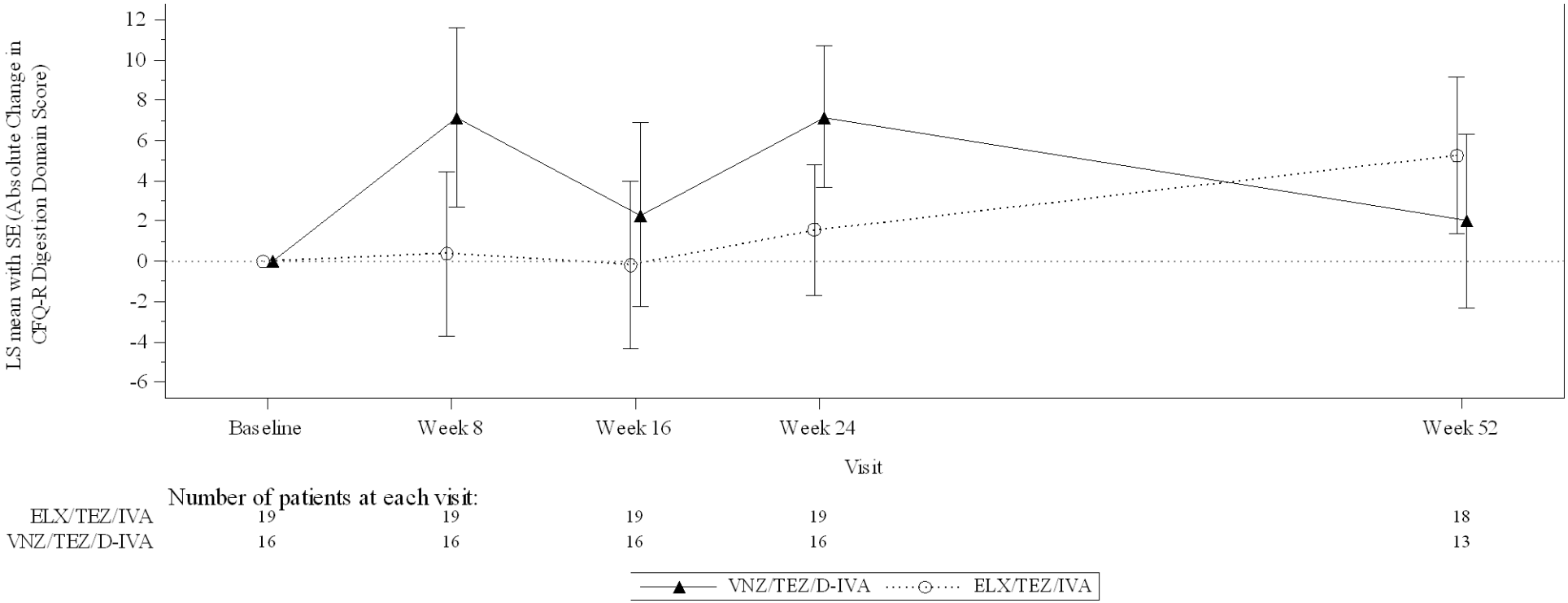
Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L



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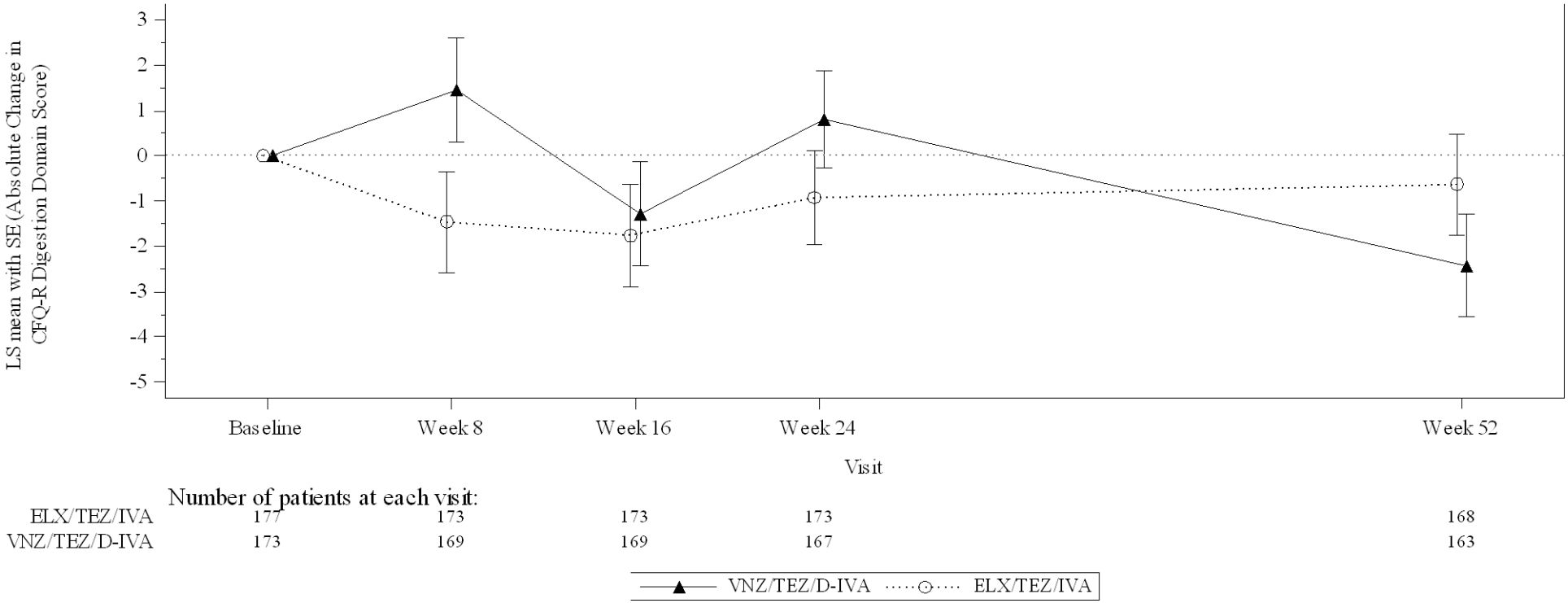
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L



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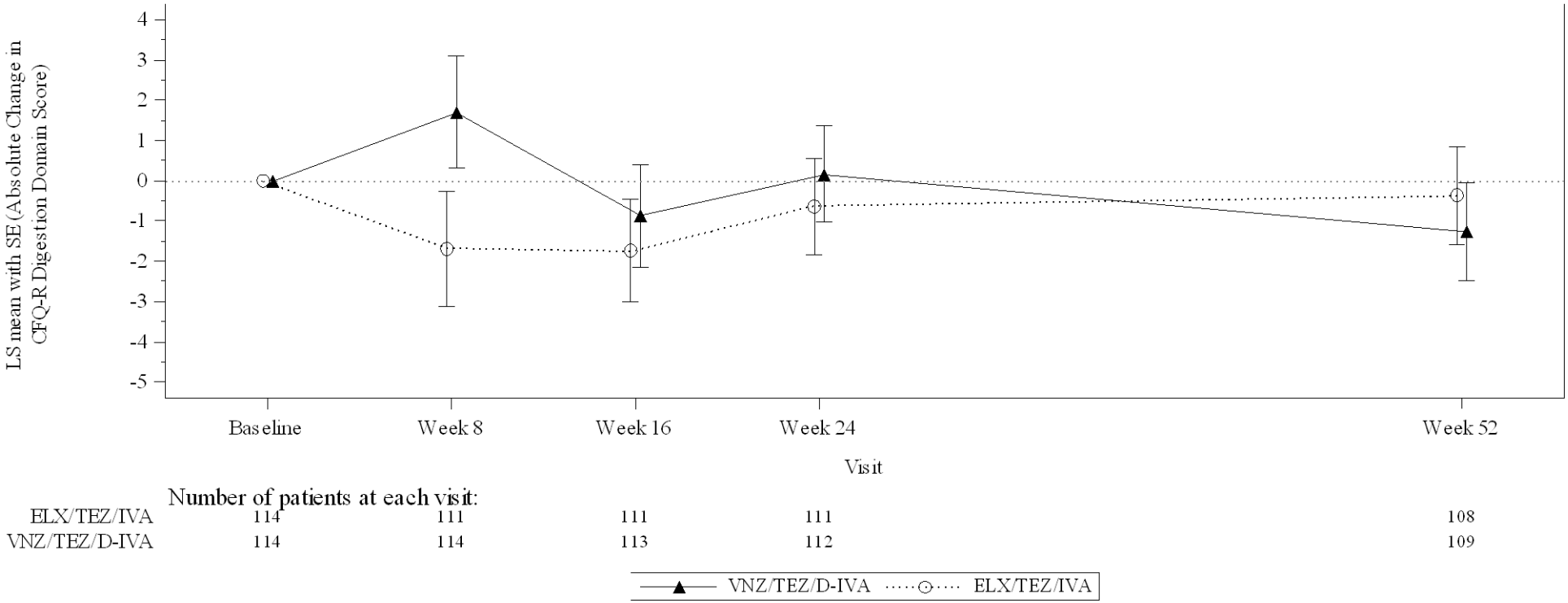
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male



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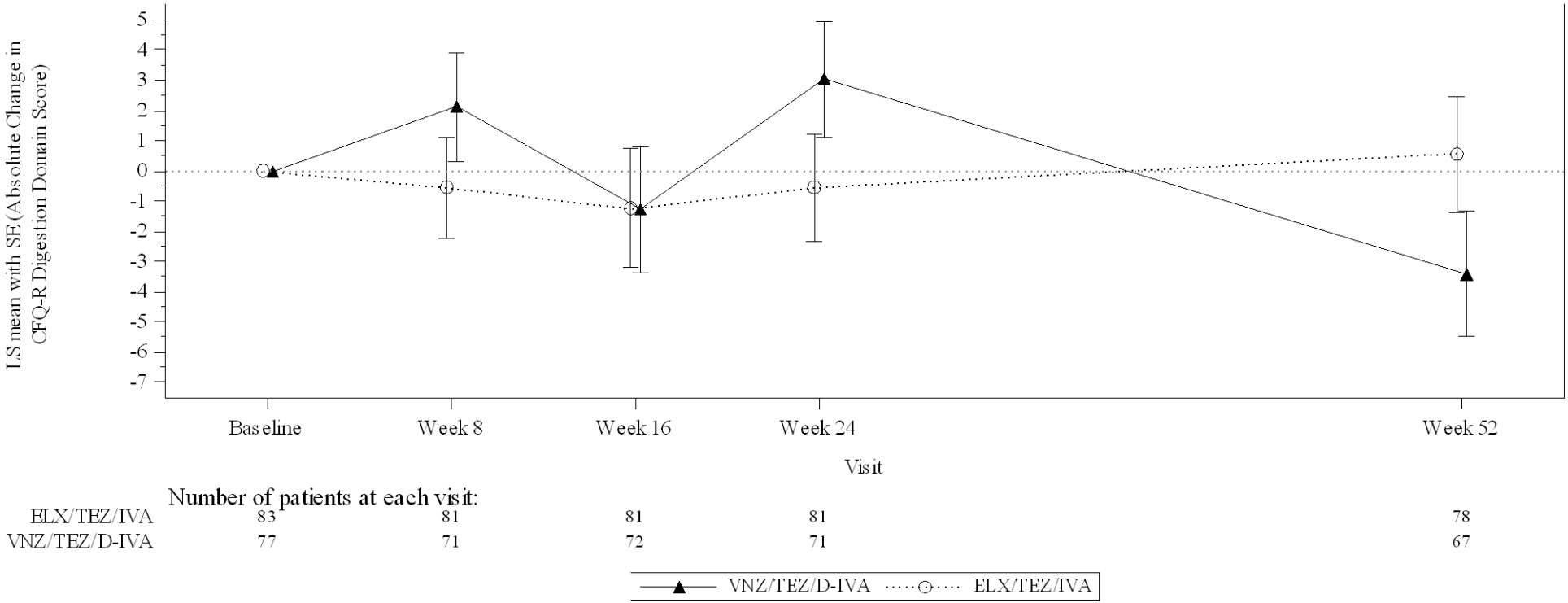
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female



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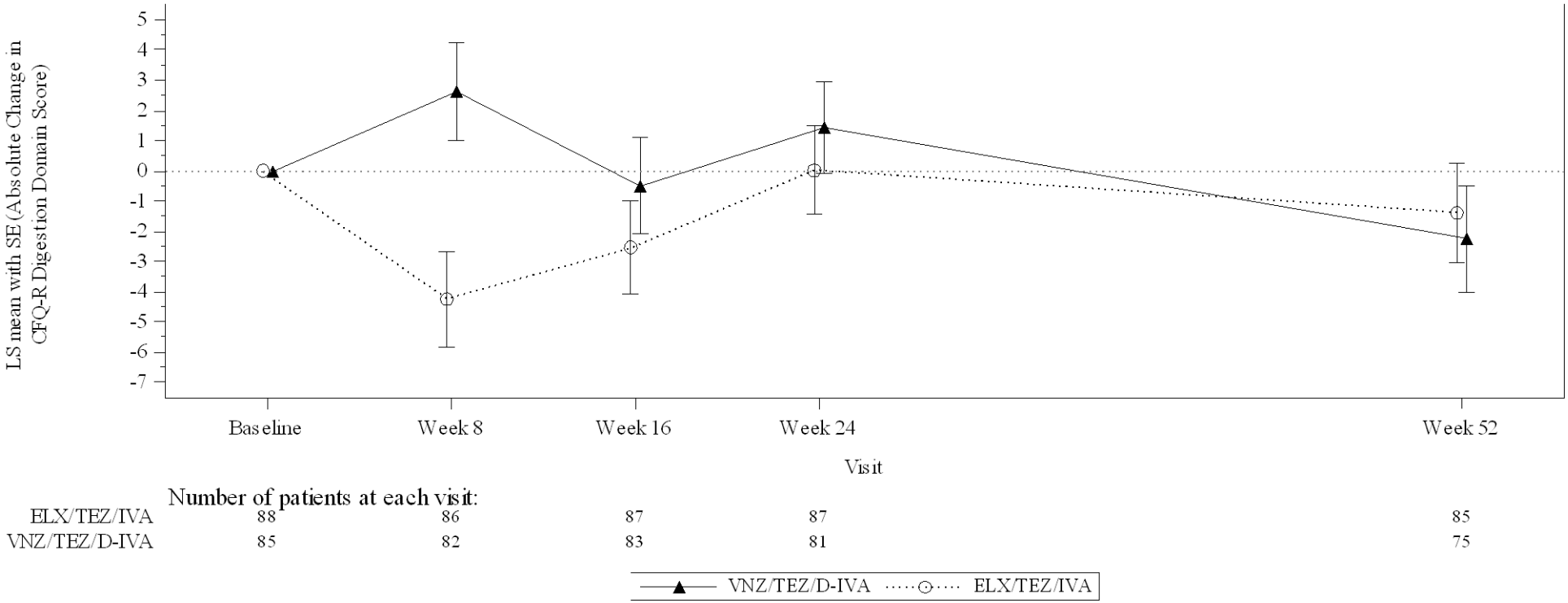
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America



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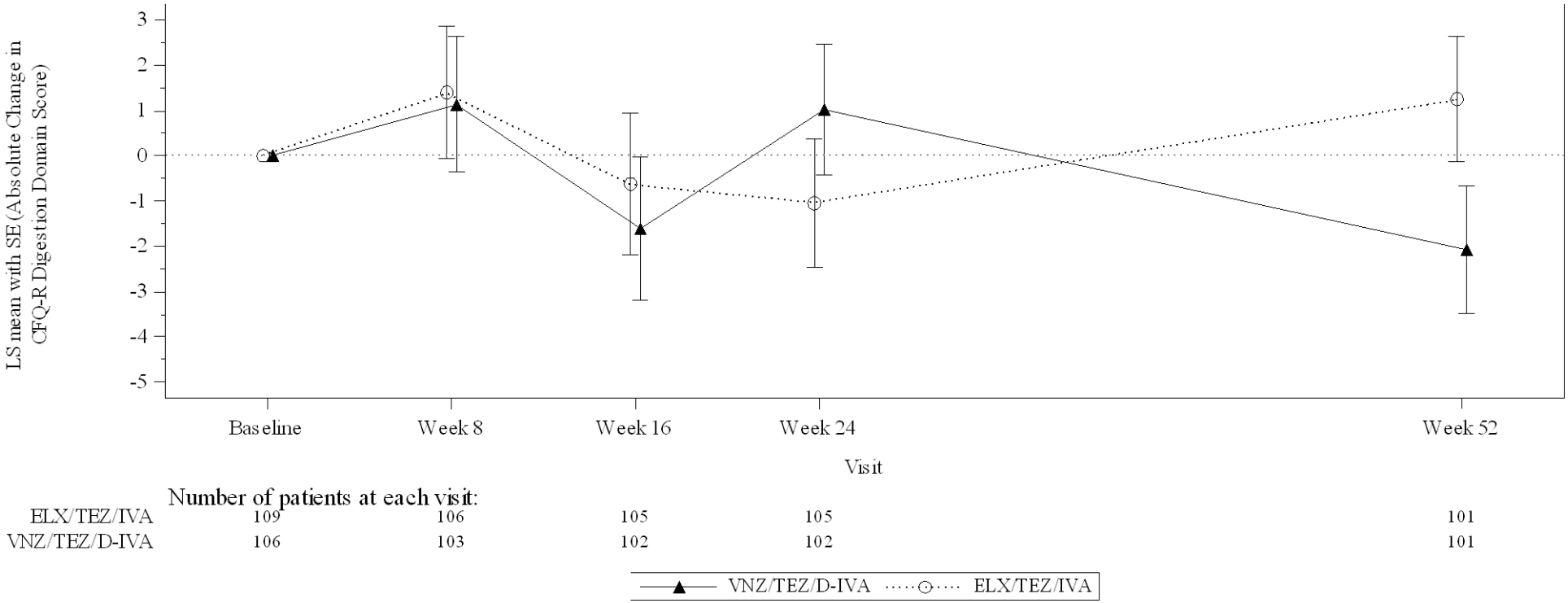
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World



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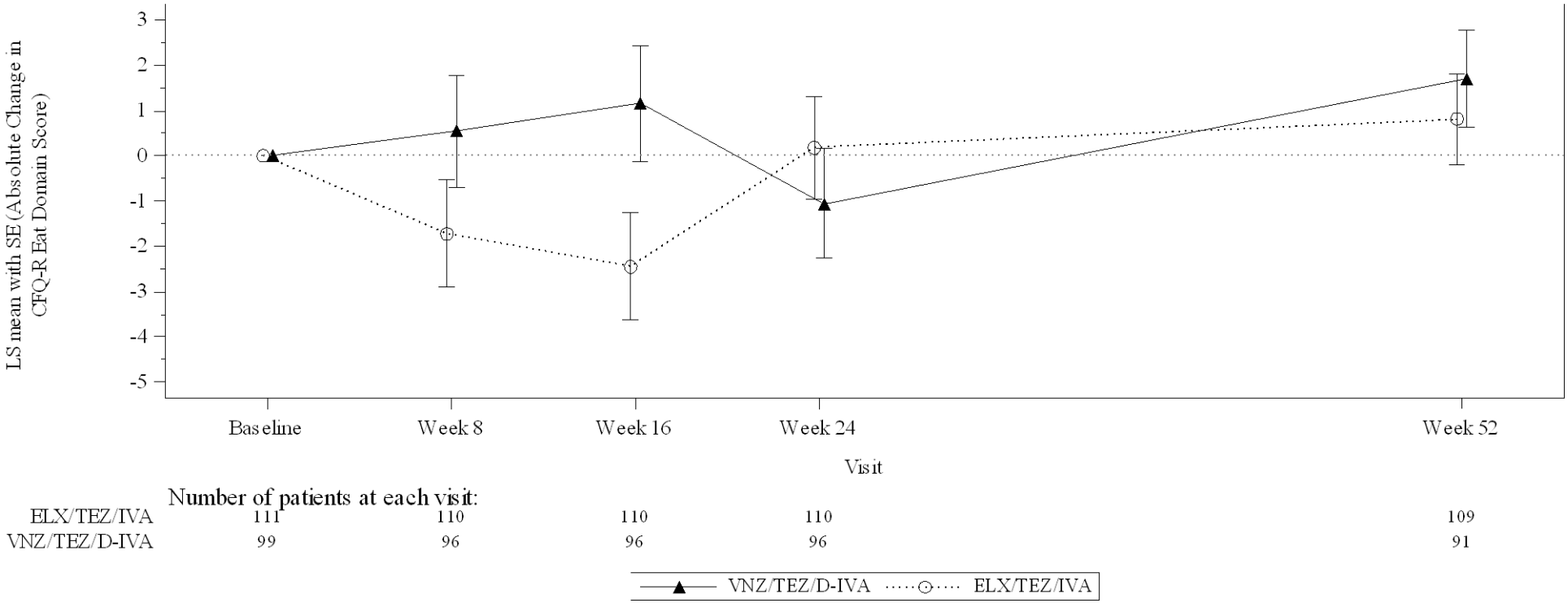
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
ppFEV$_1$ at baseline <70 %



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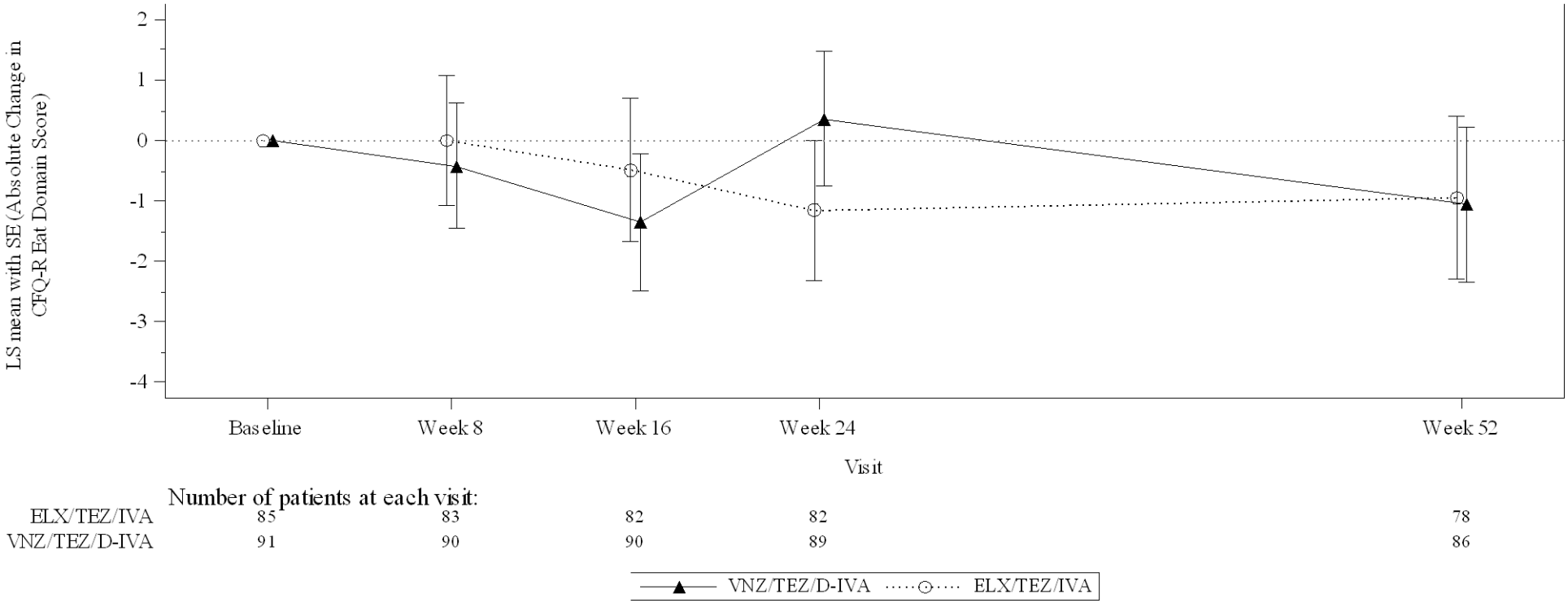
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
ppFEV$_1$ at baseline ≥70 %



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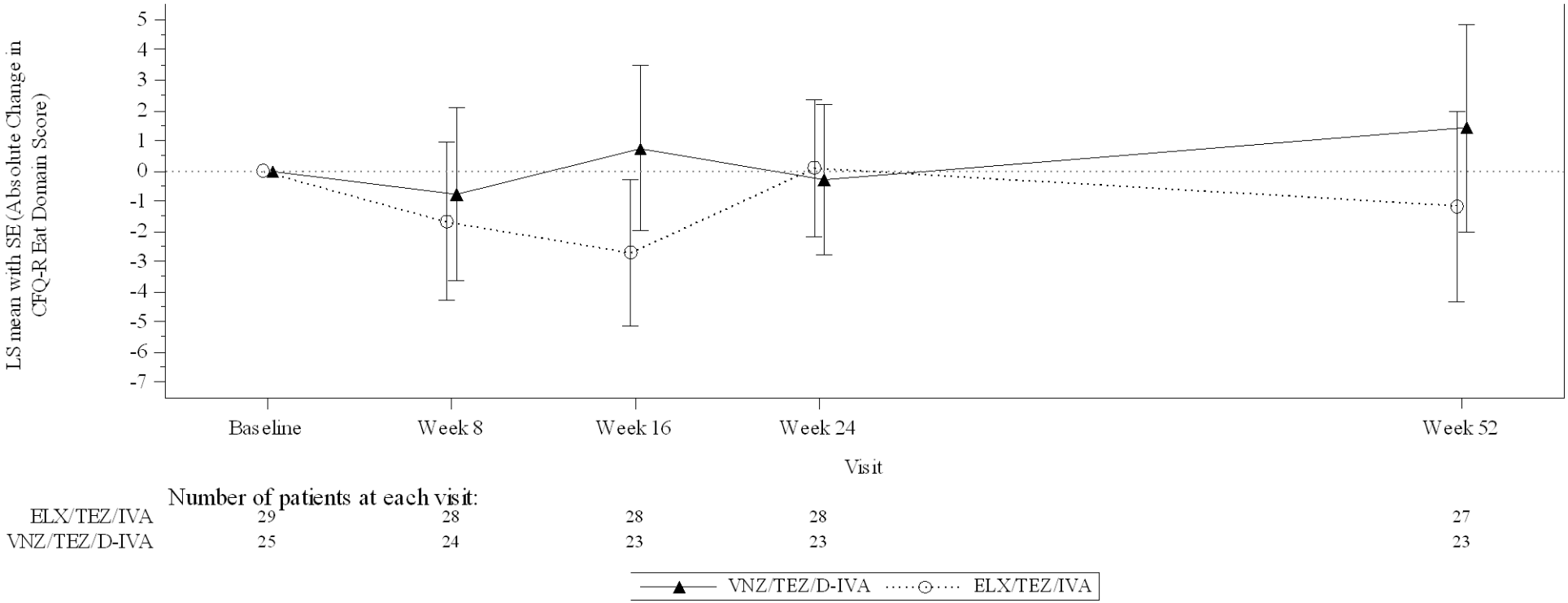
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years



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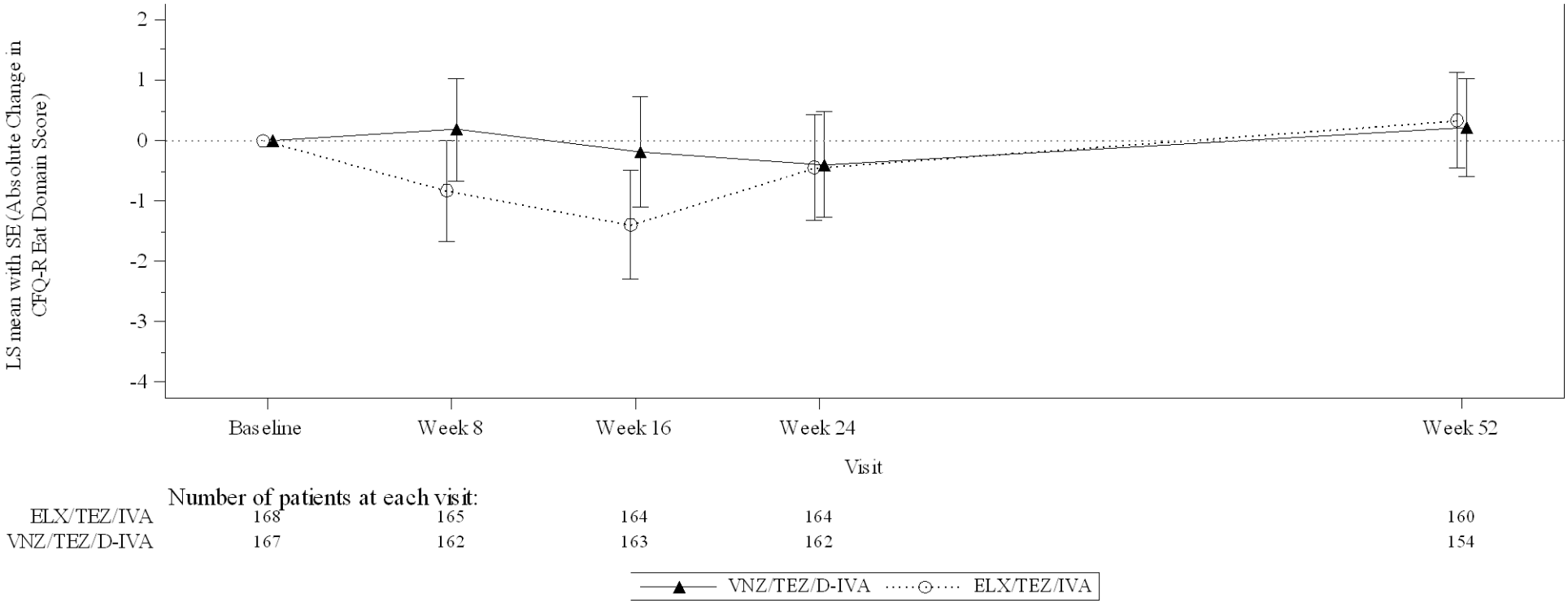
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years



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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

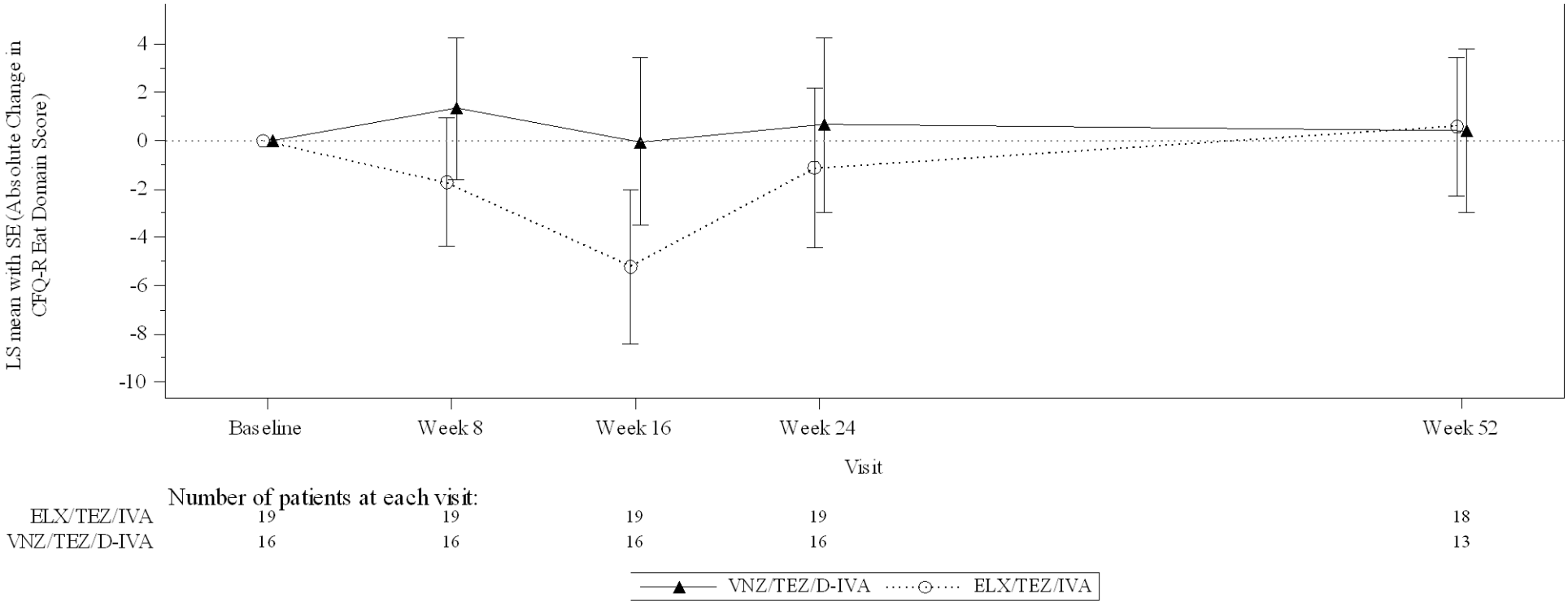

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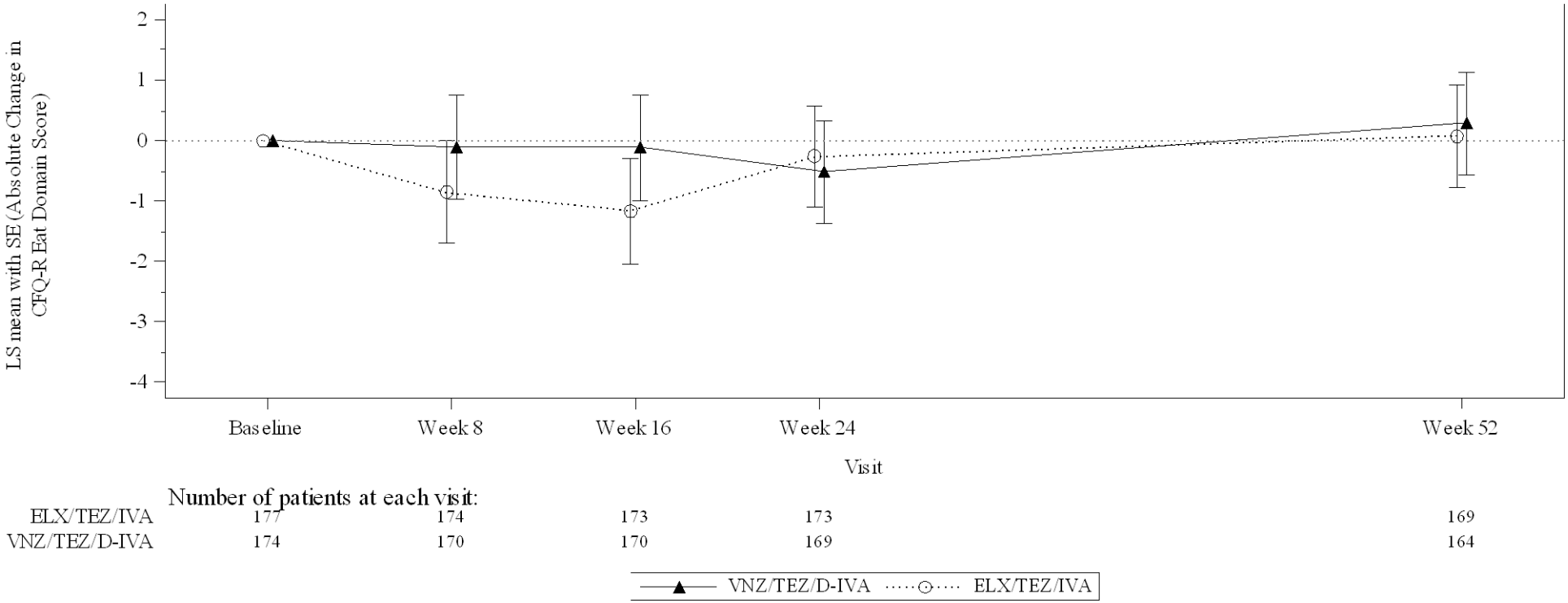
Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L



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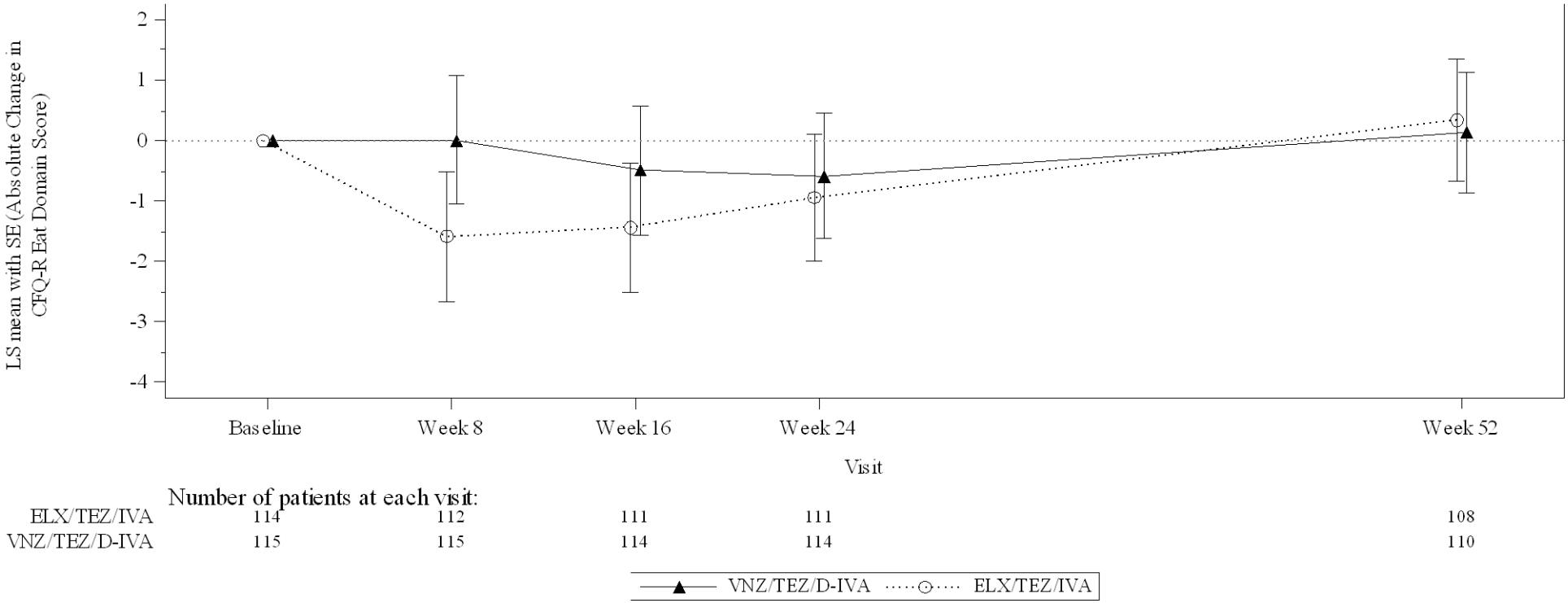
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male



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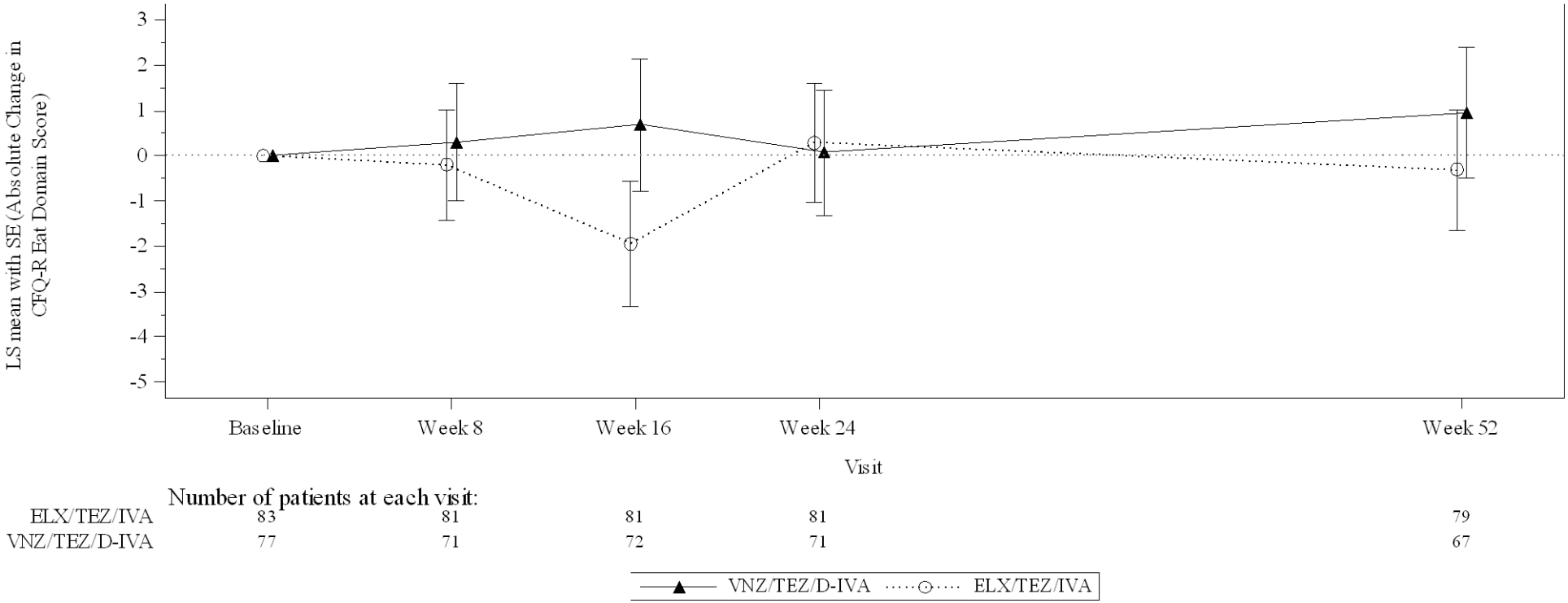
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female



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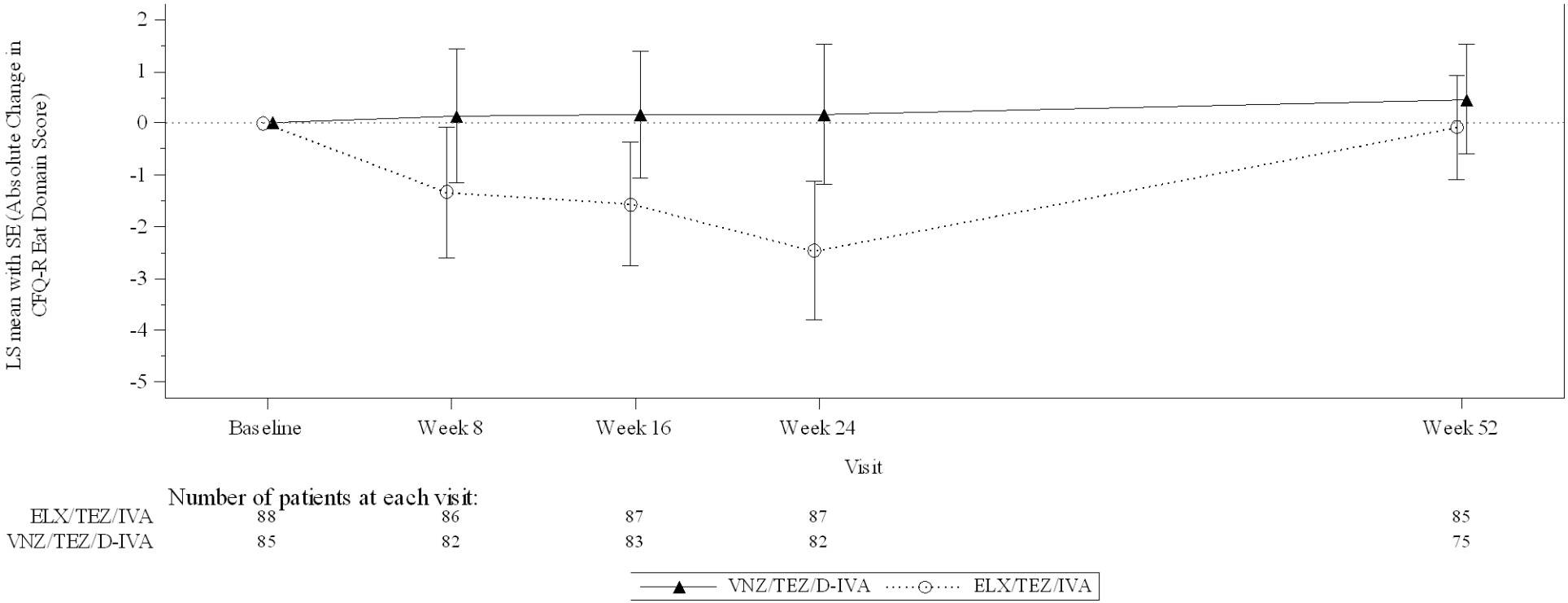
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America



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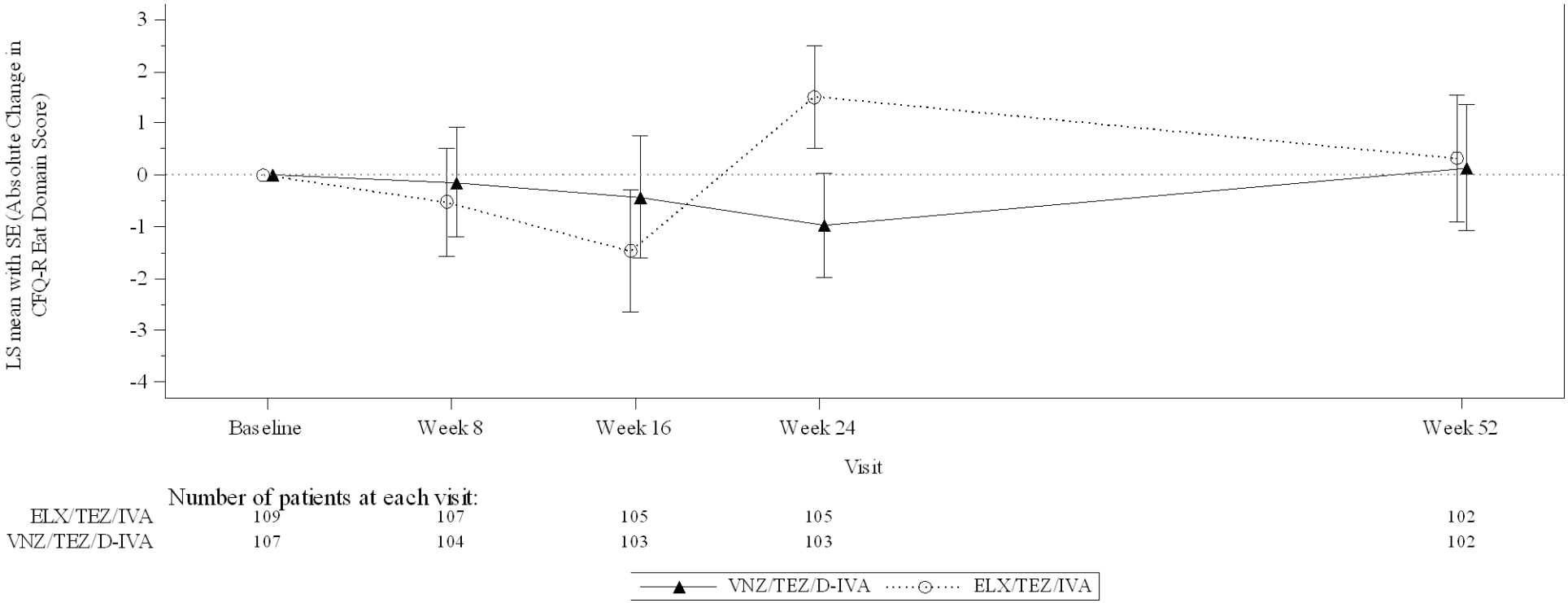
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World



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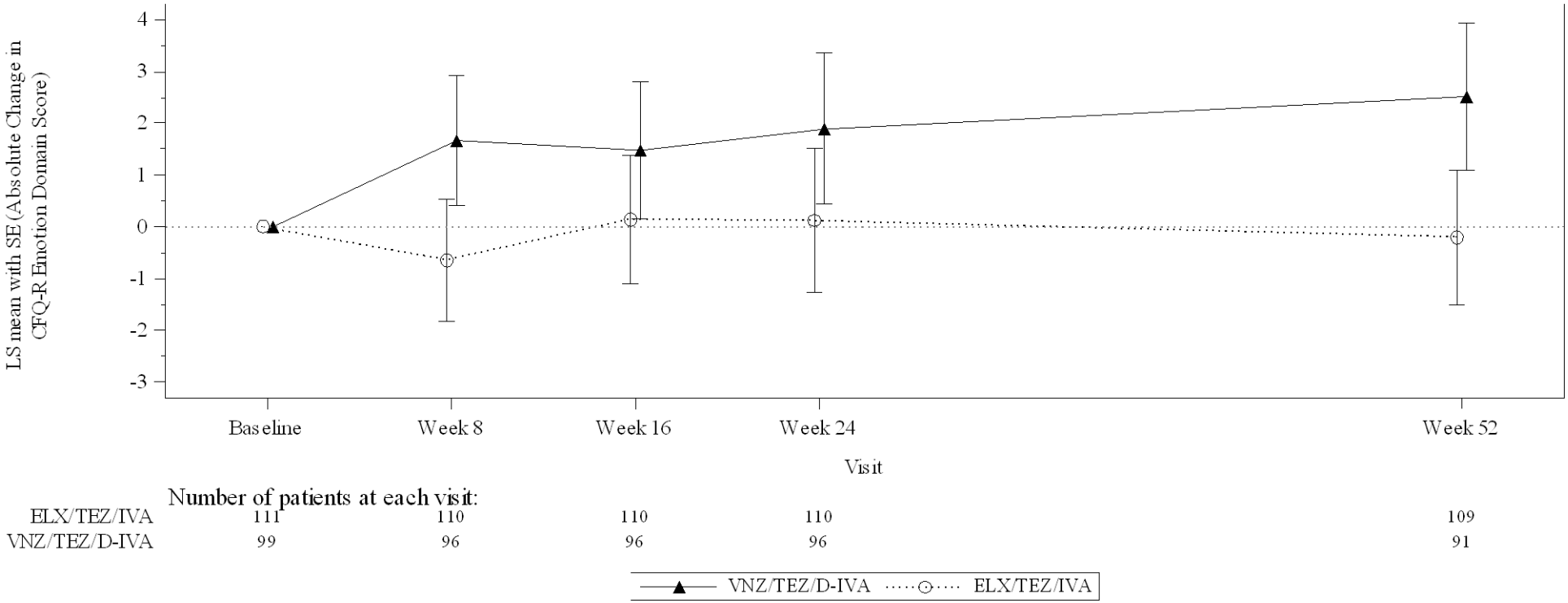
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
ppFEV$_1$ at baseline <70 %



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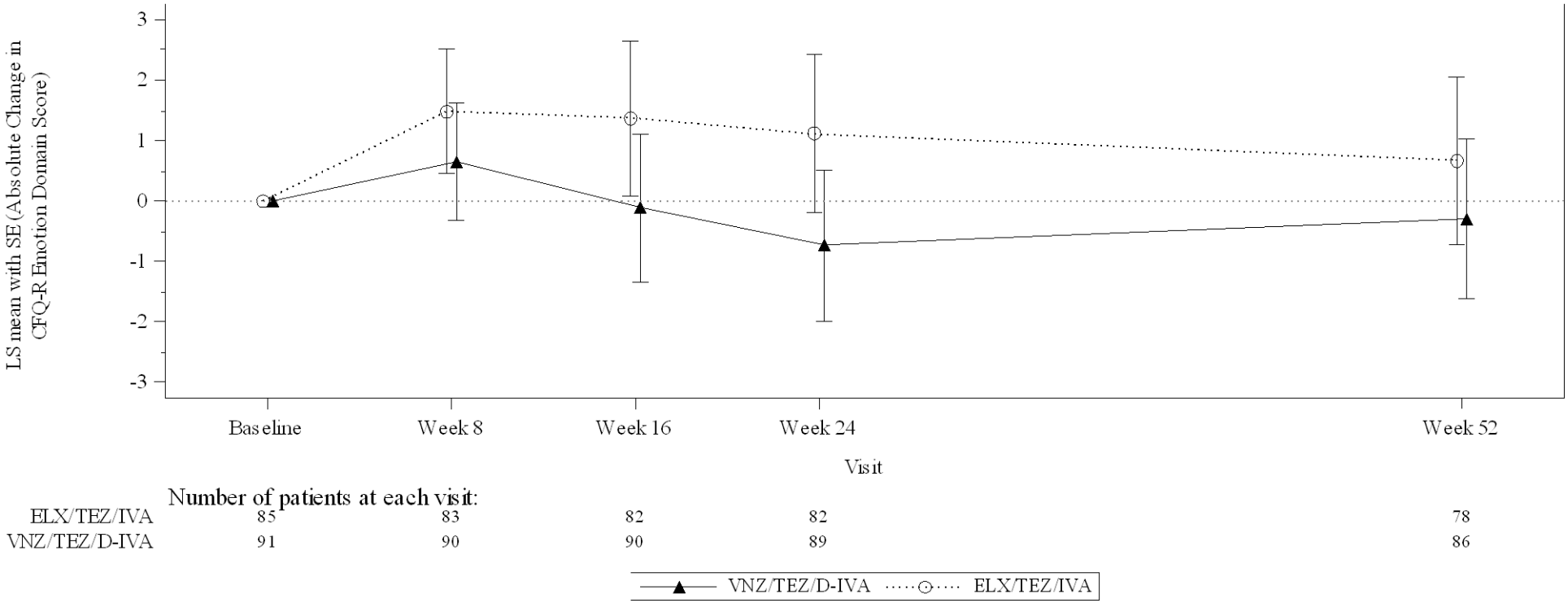
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
ppFEV$_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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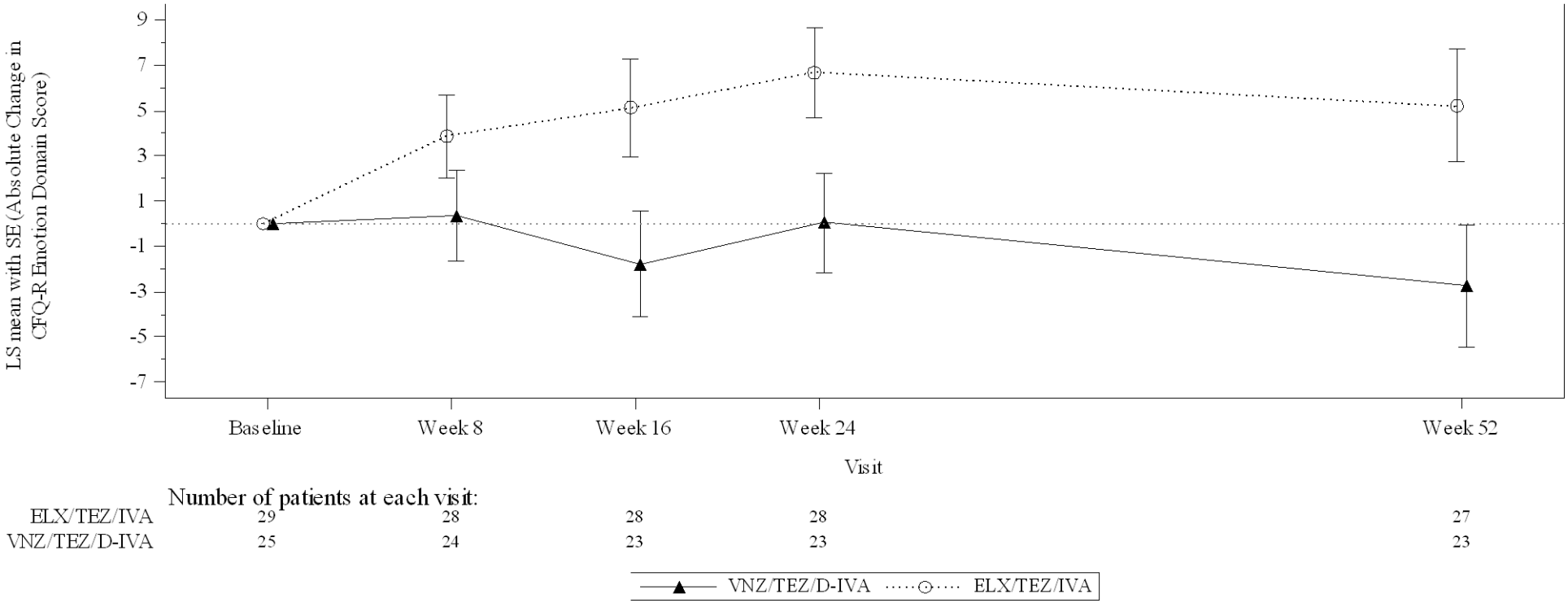
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years



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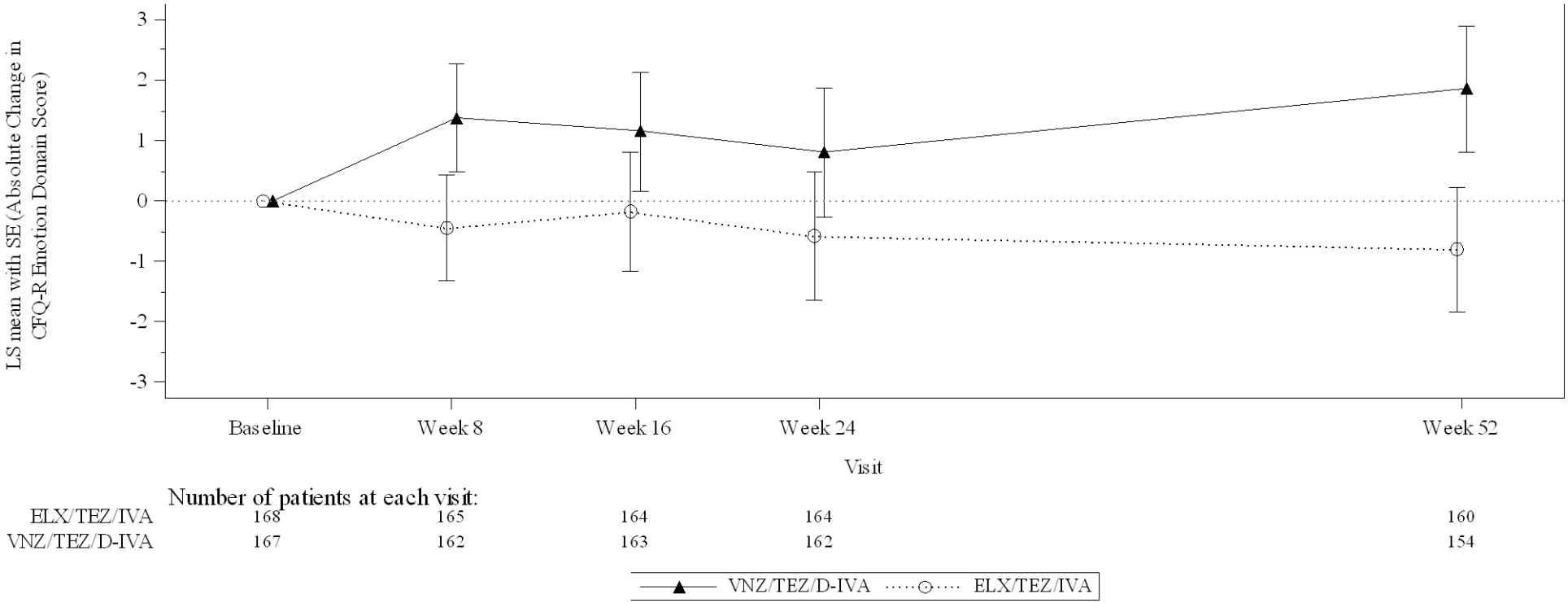
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years



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- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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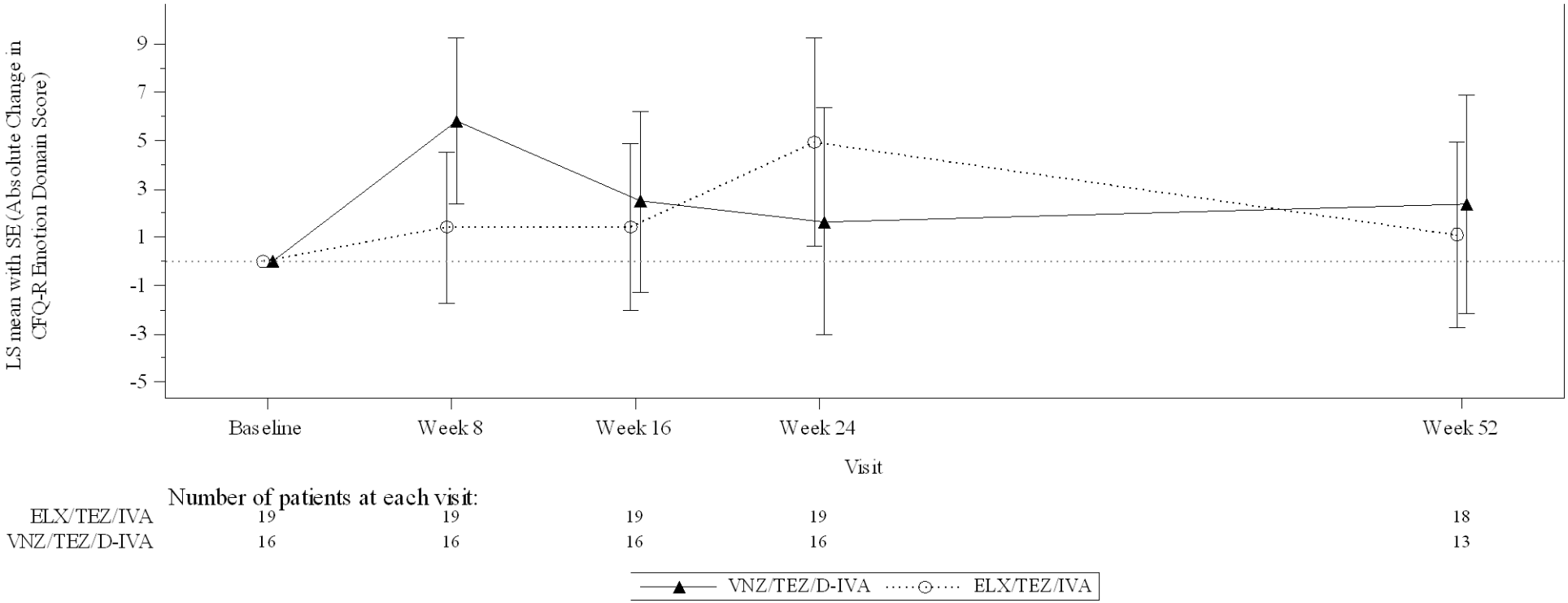
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L



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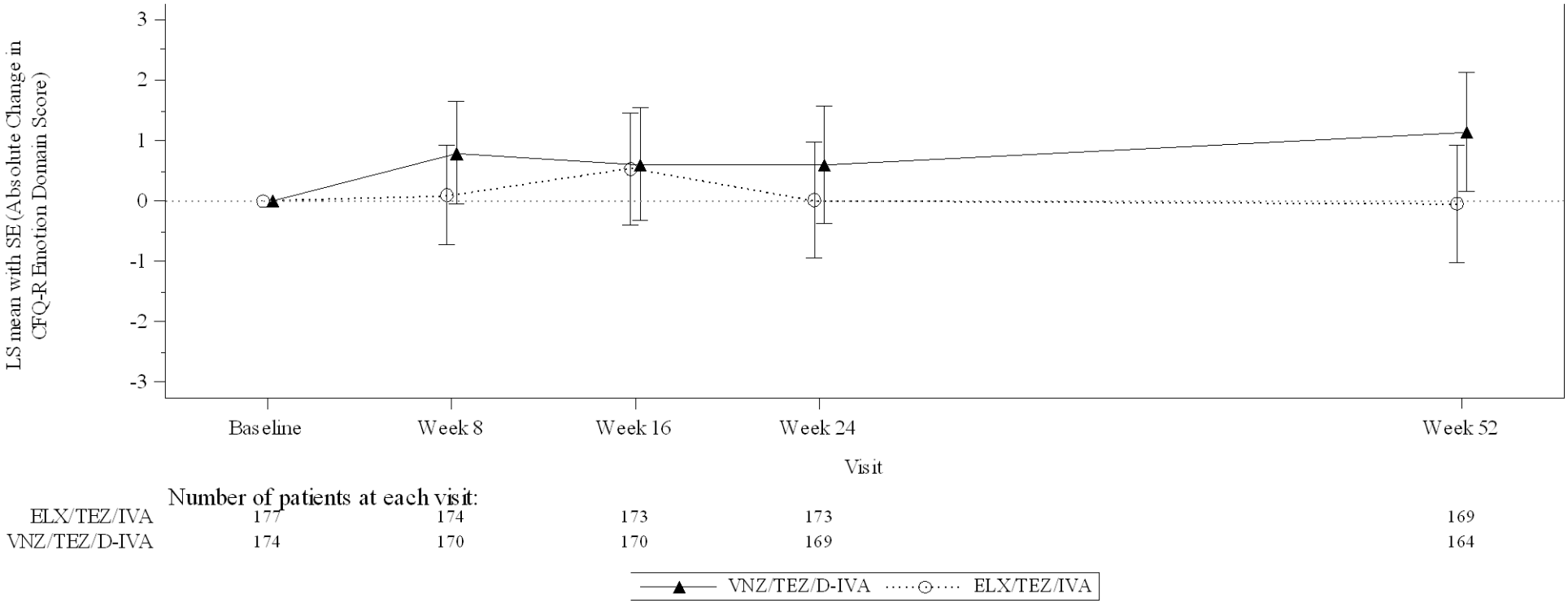
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L



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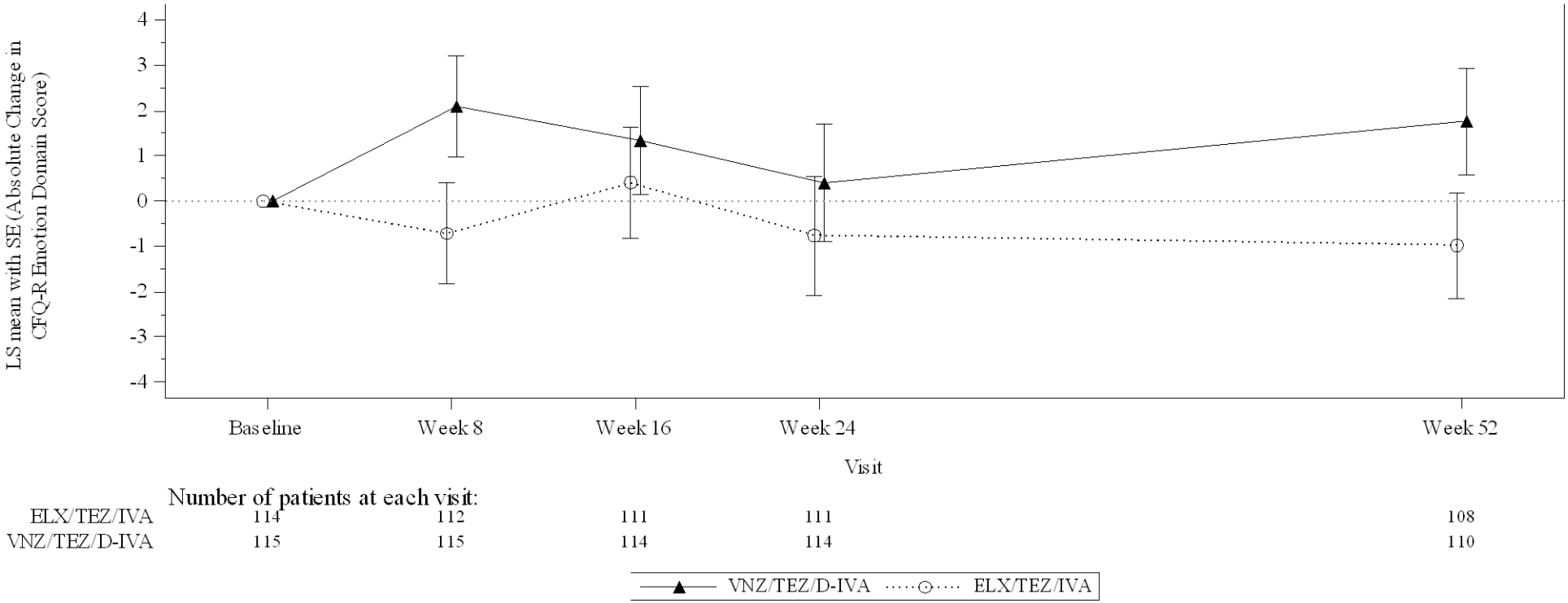
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male



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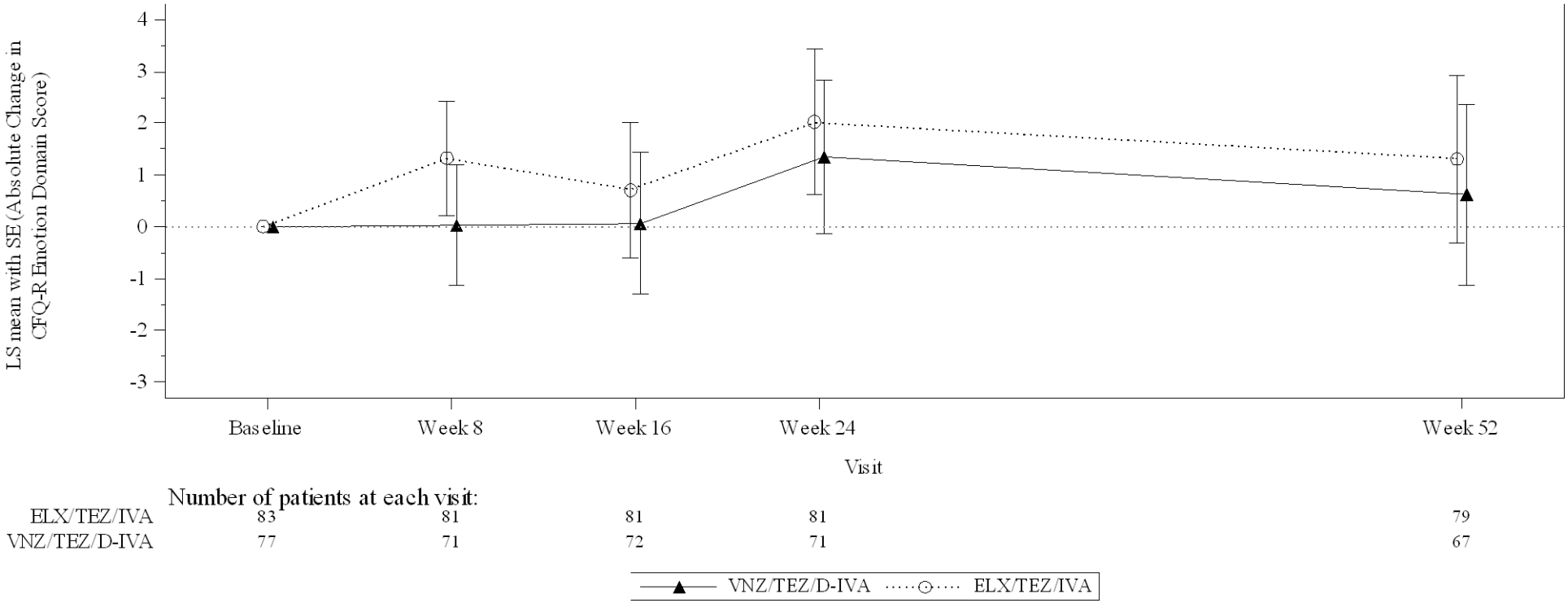
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female



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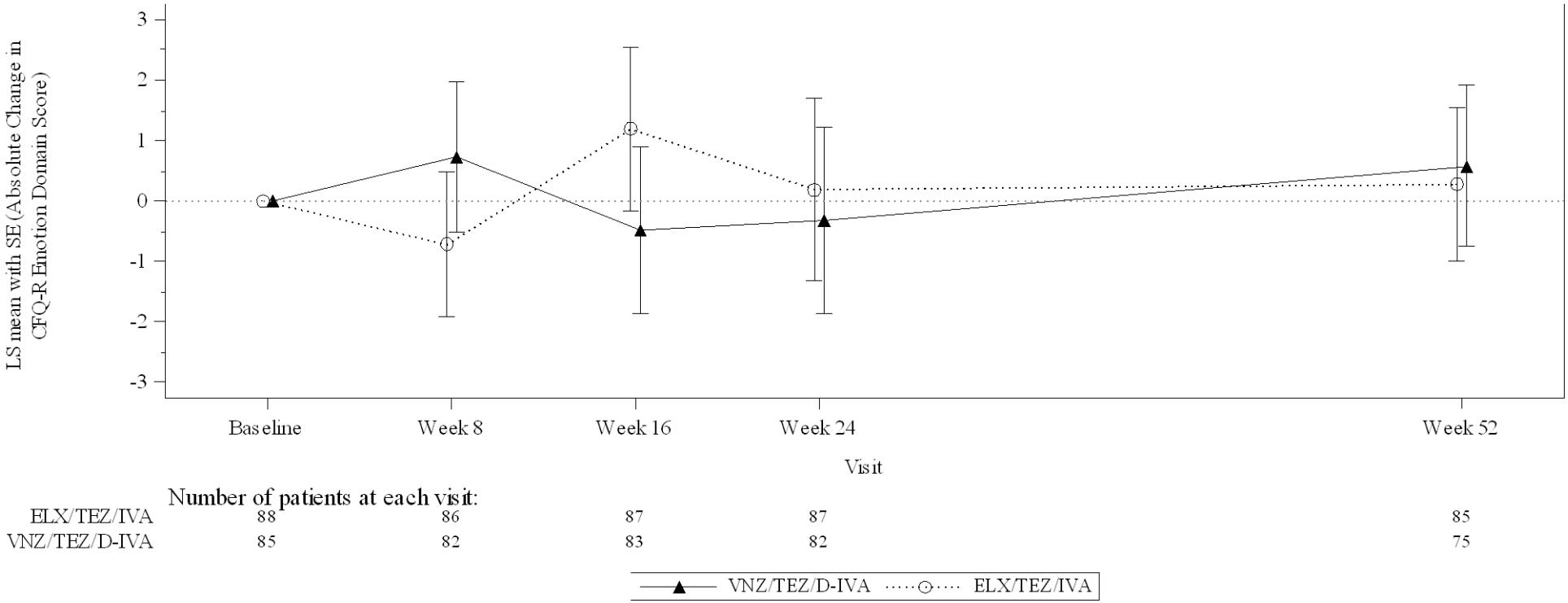
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America



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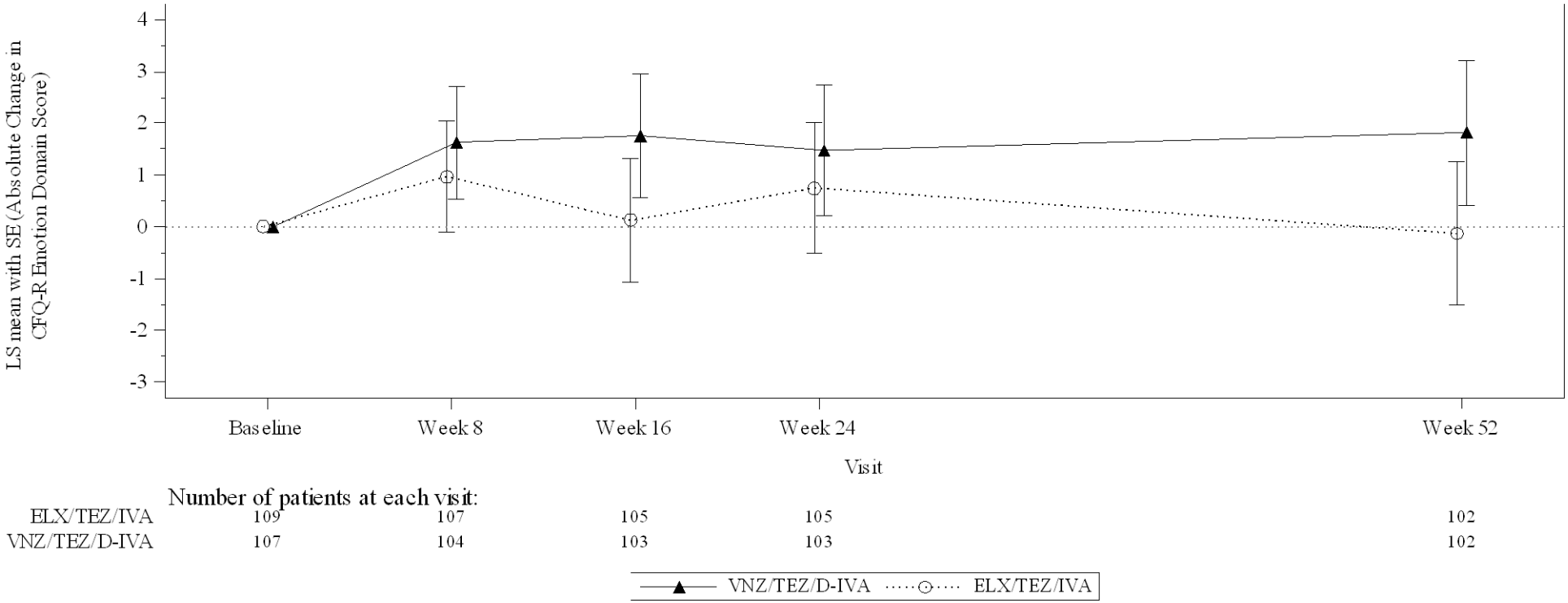
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World



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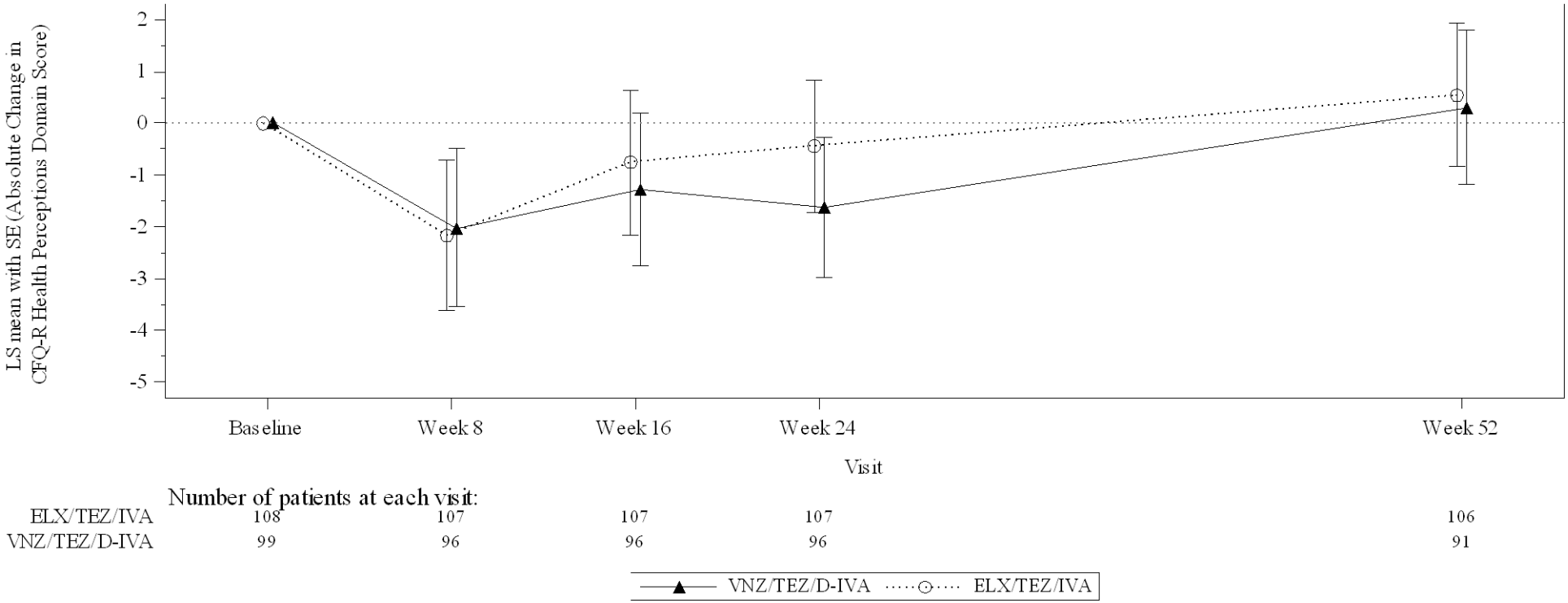
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
ppFEV$_1$ at baseline <70 %



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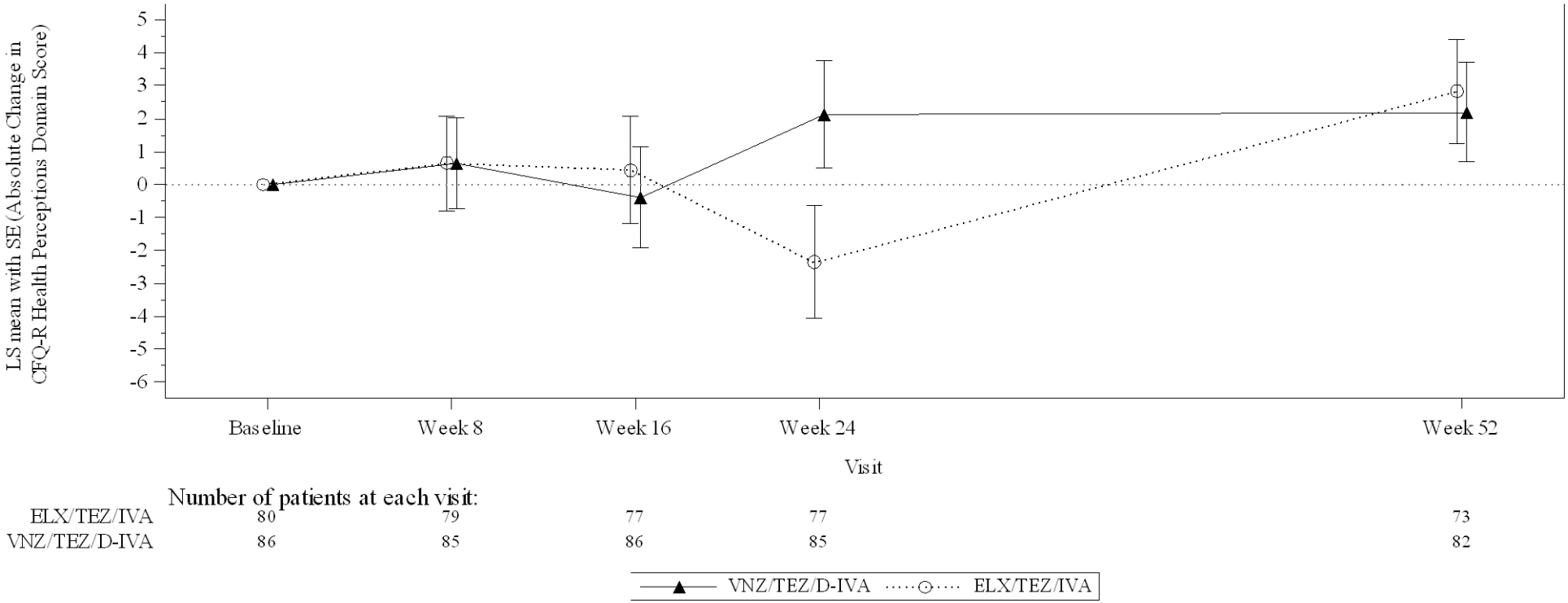
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
ppFEV$_1$ at baseline ≥70 %



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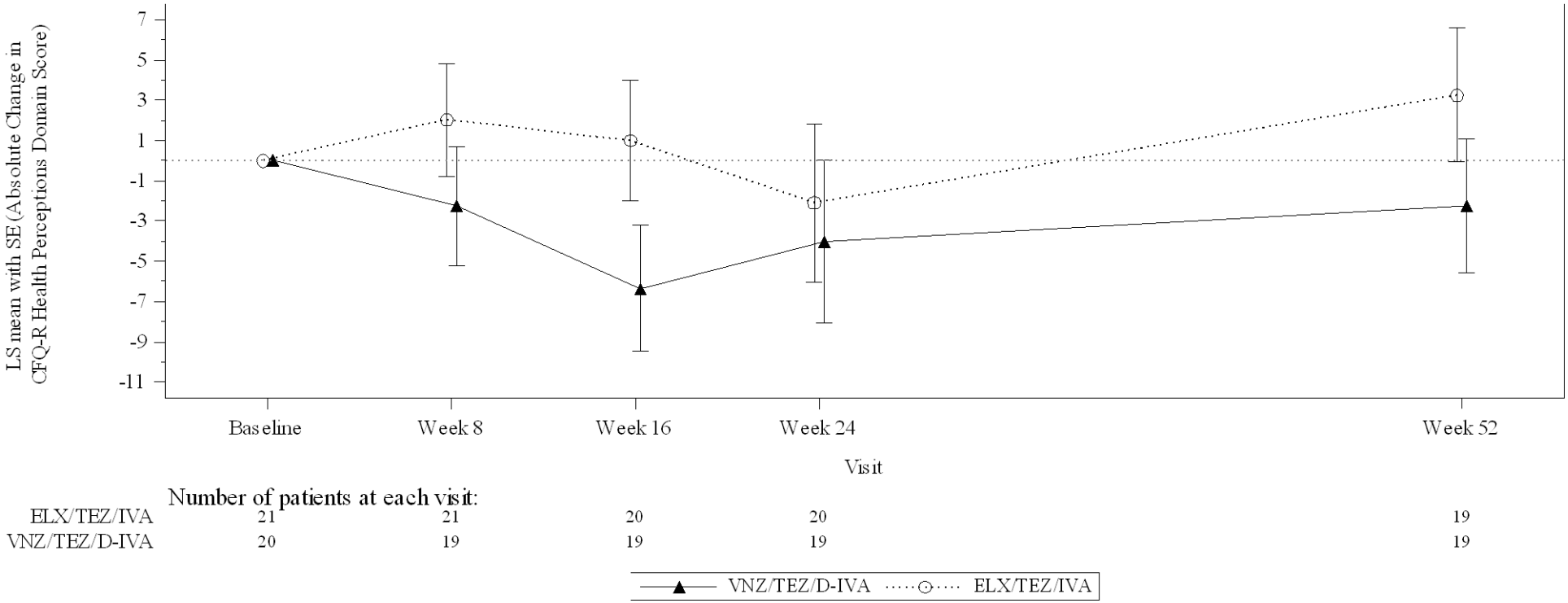
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years



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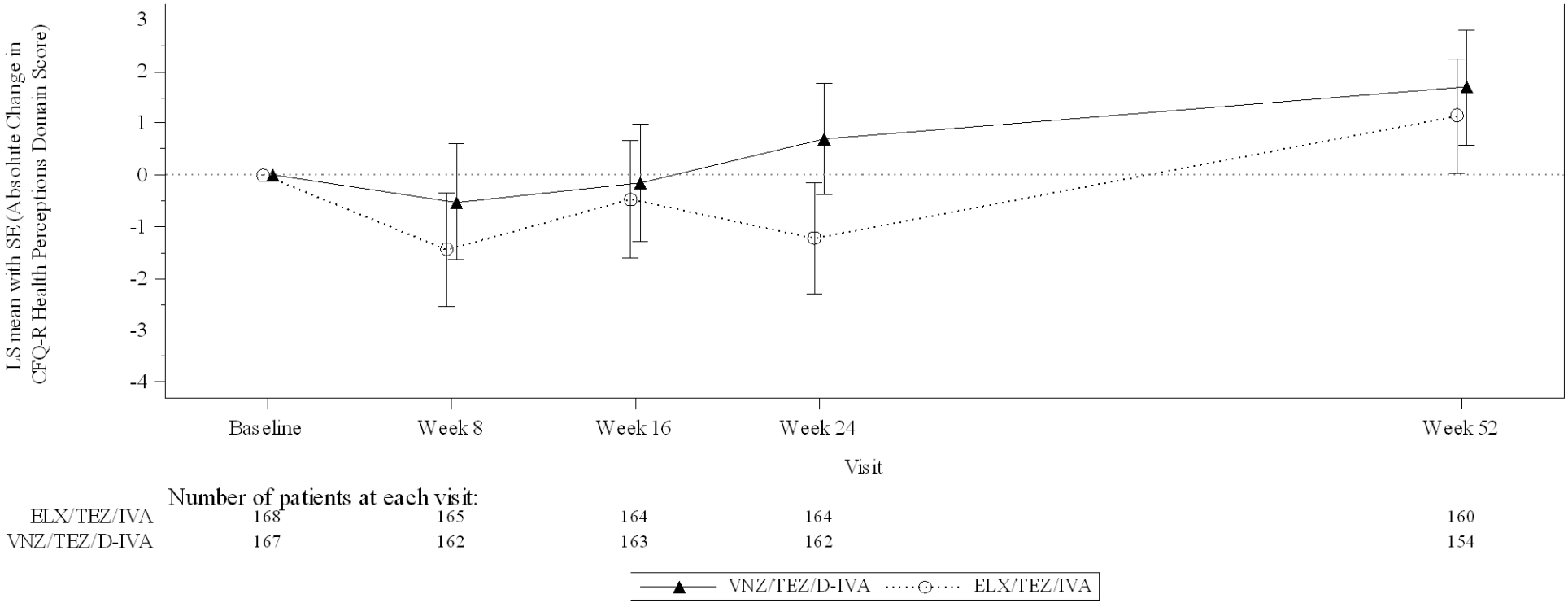
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years



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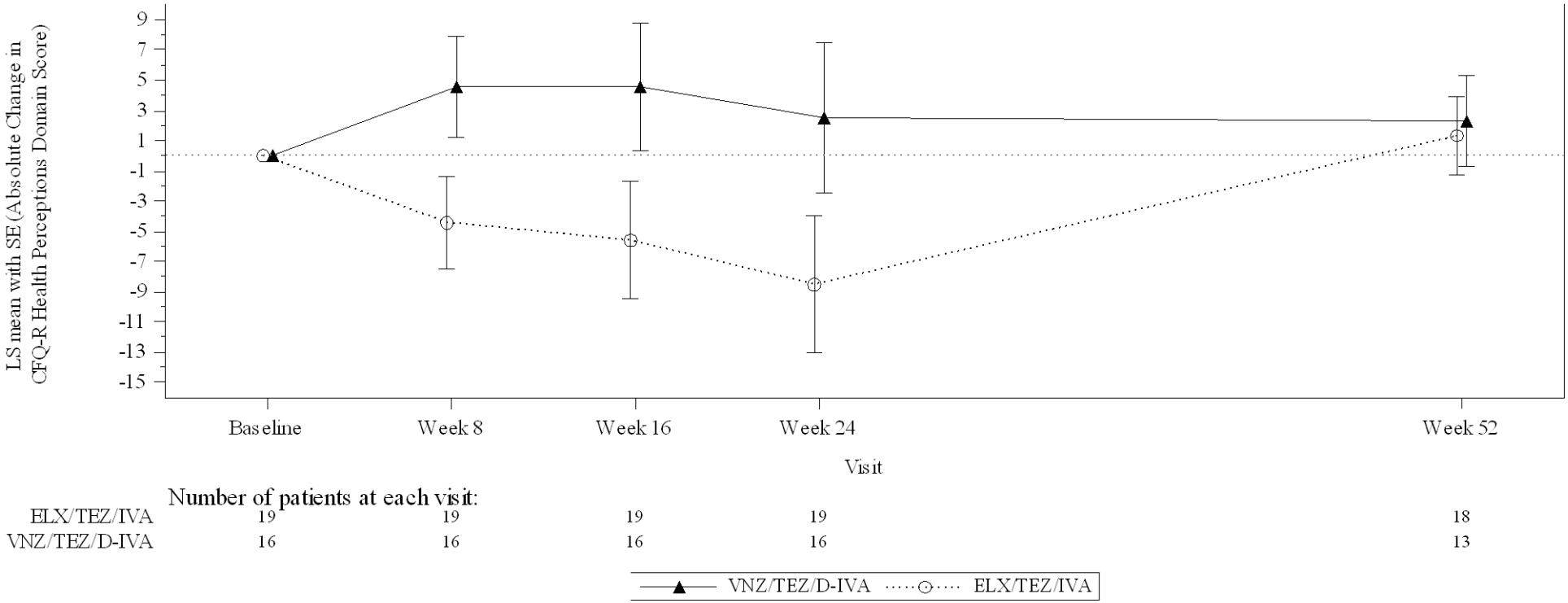
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L



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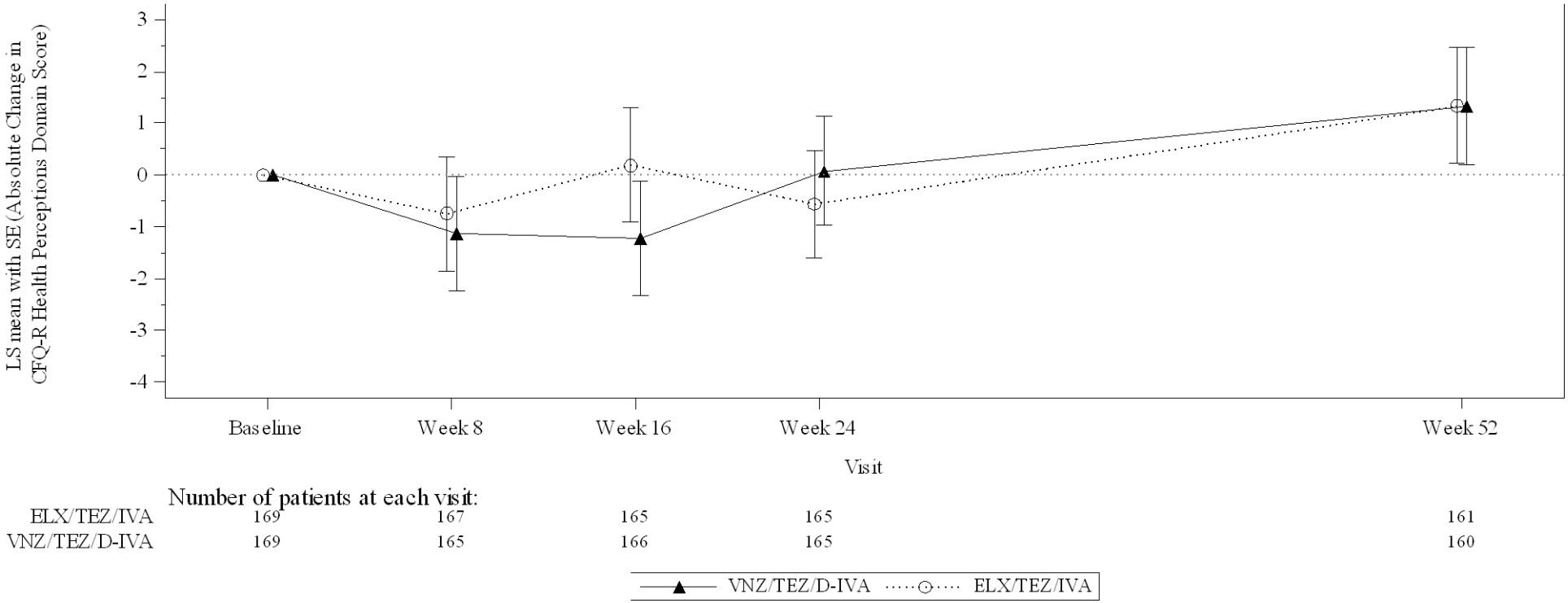
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L



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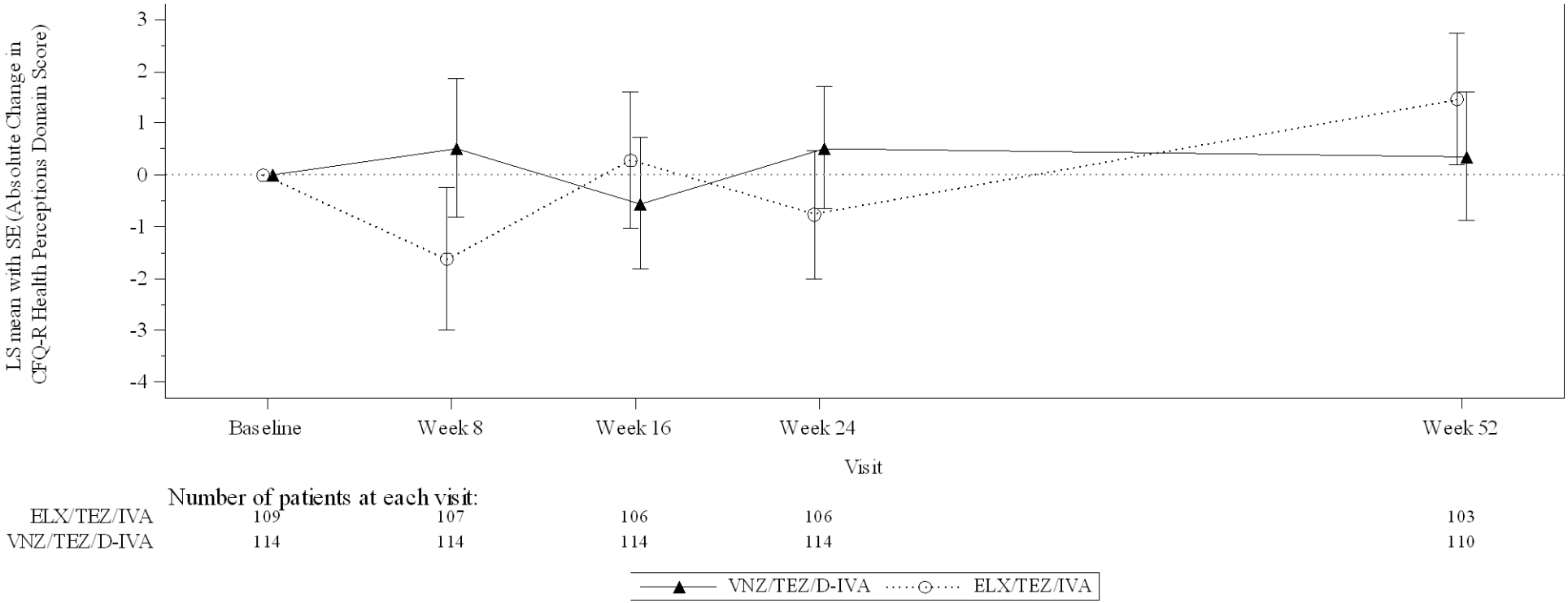
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male



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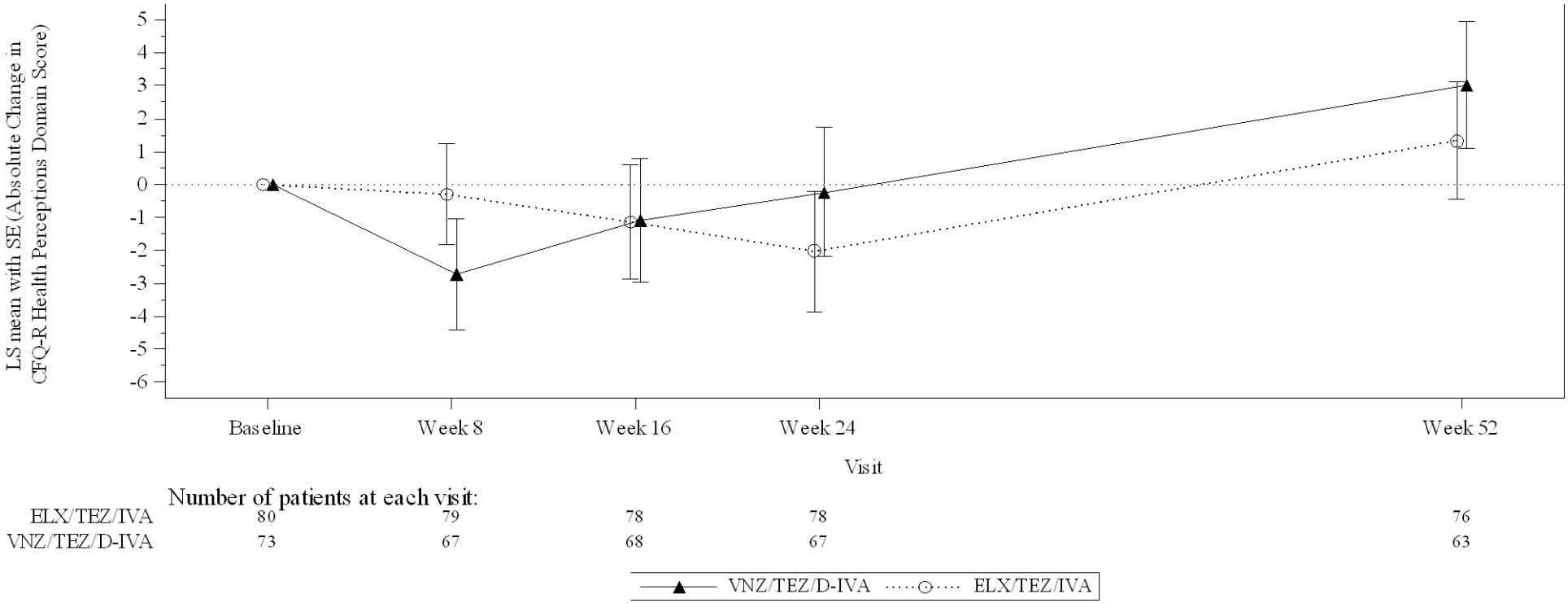
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female



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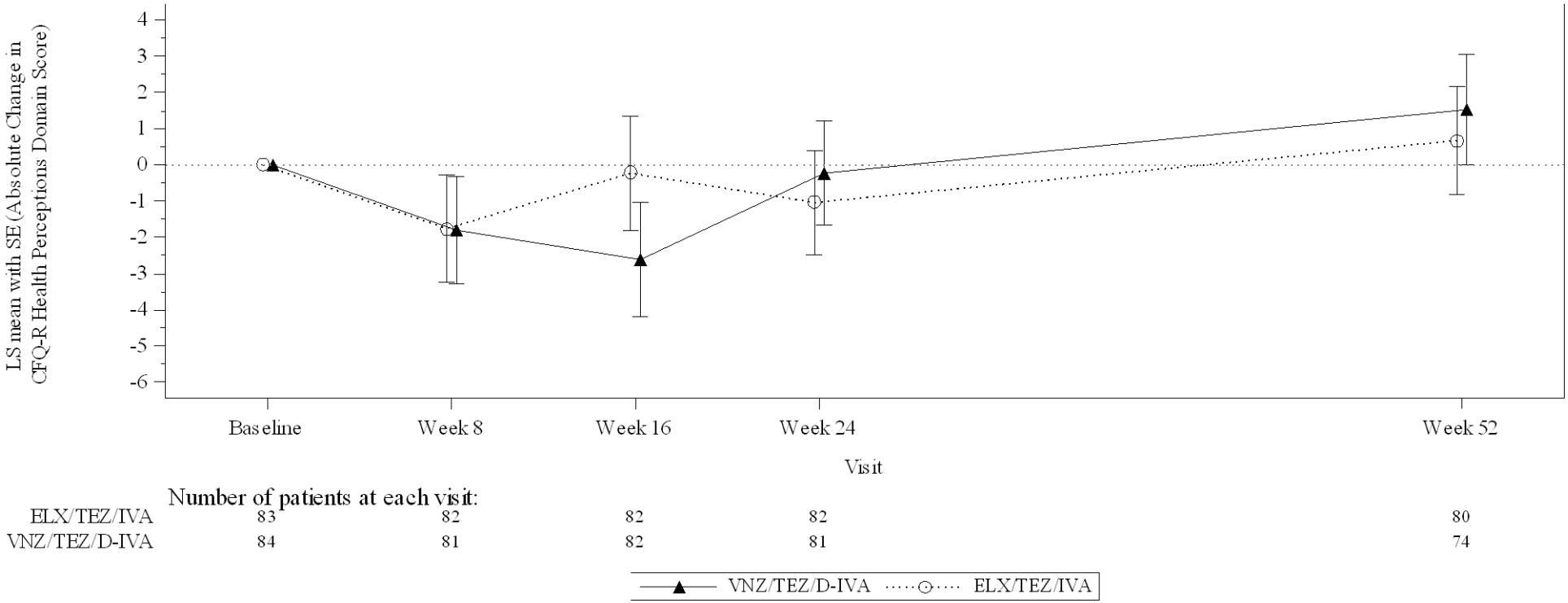
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America



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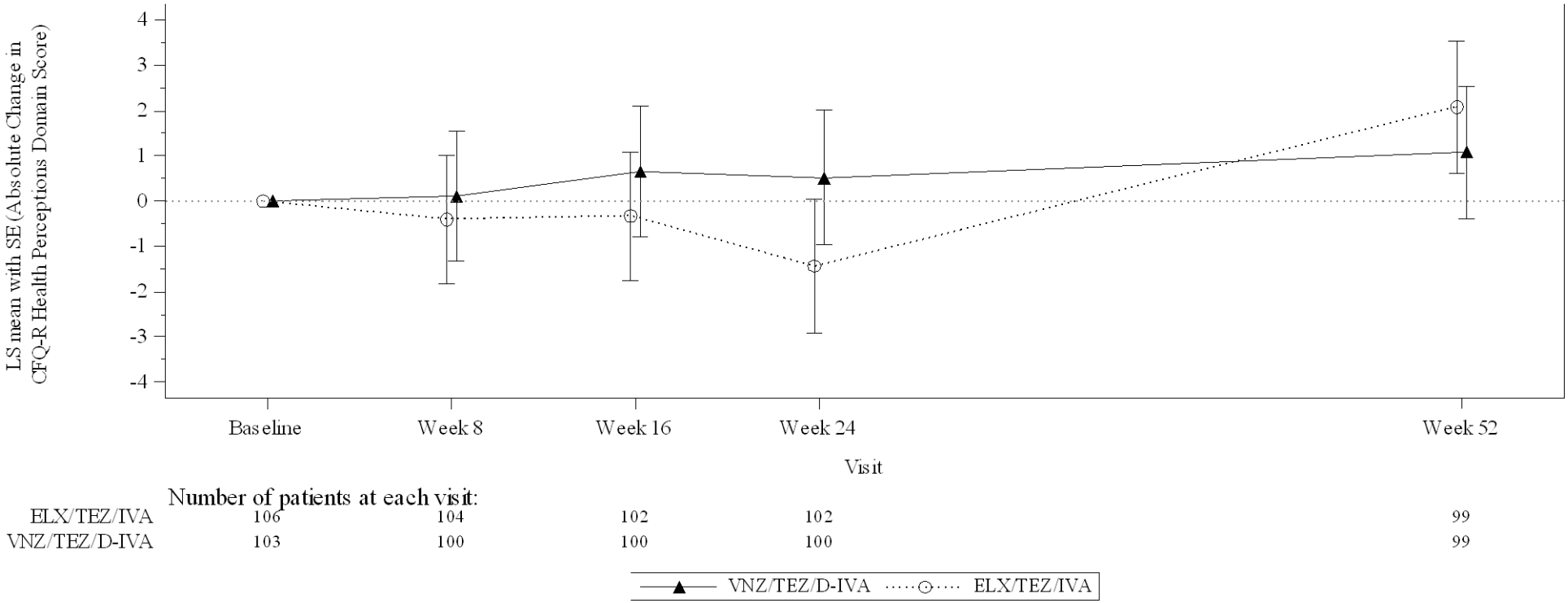
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World



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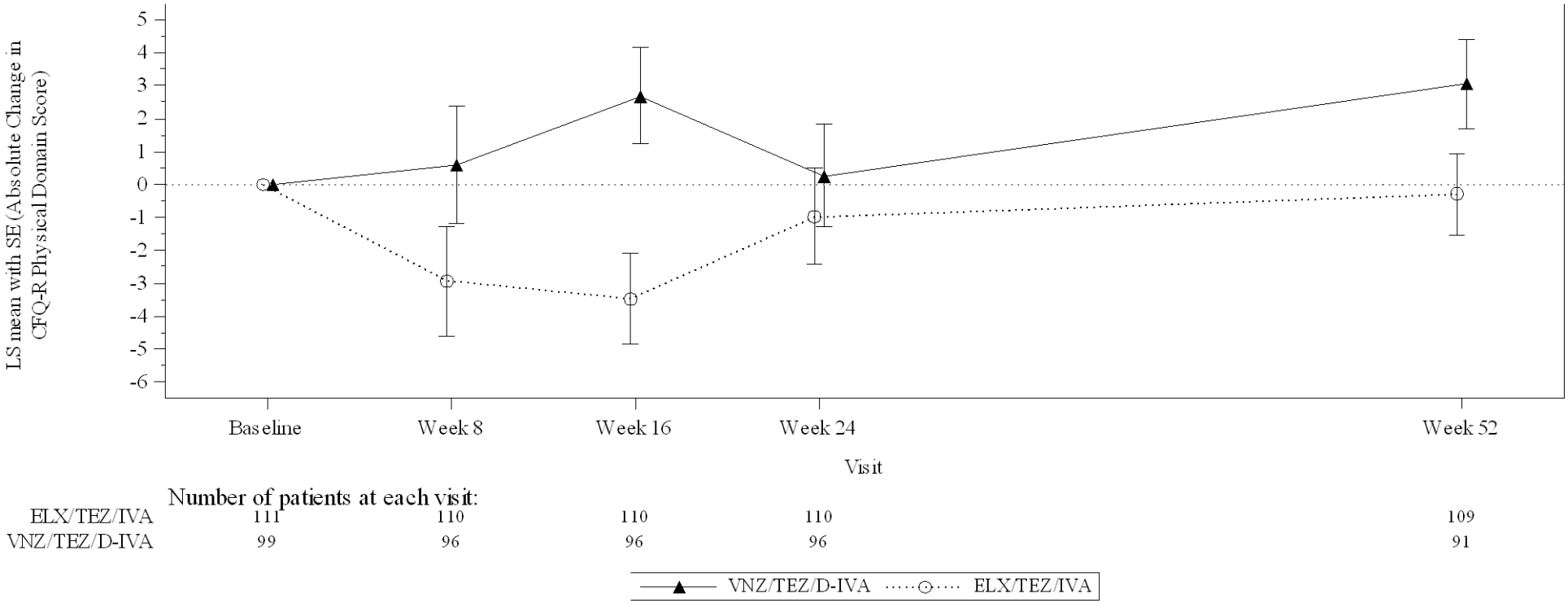
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
ppFEV$_1$ at baseline <70 %



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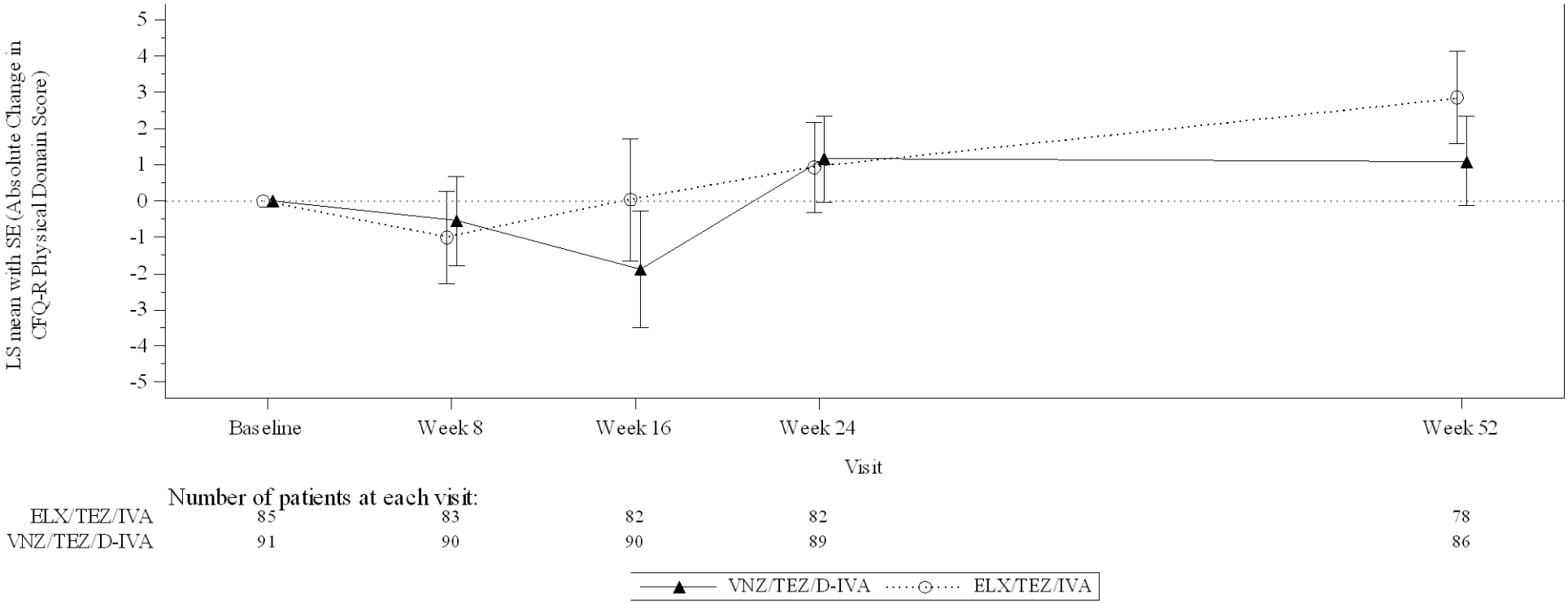
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
ppFEV$_1$ at baseline ≥70 %



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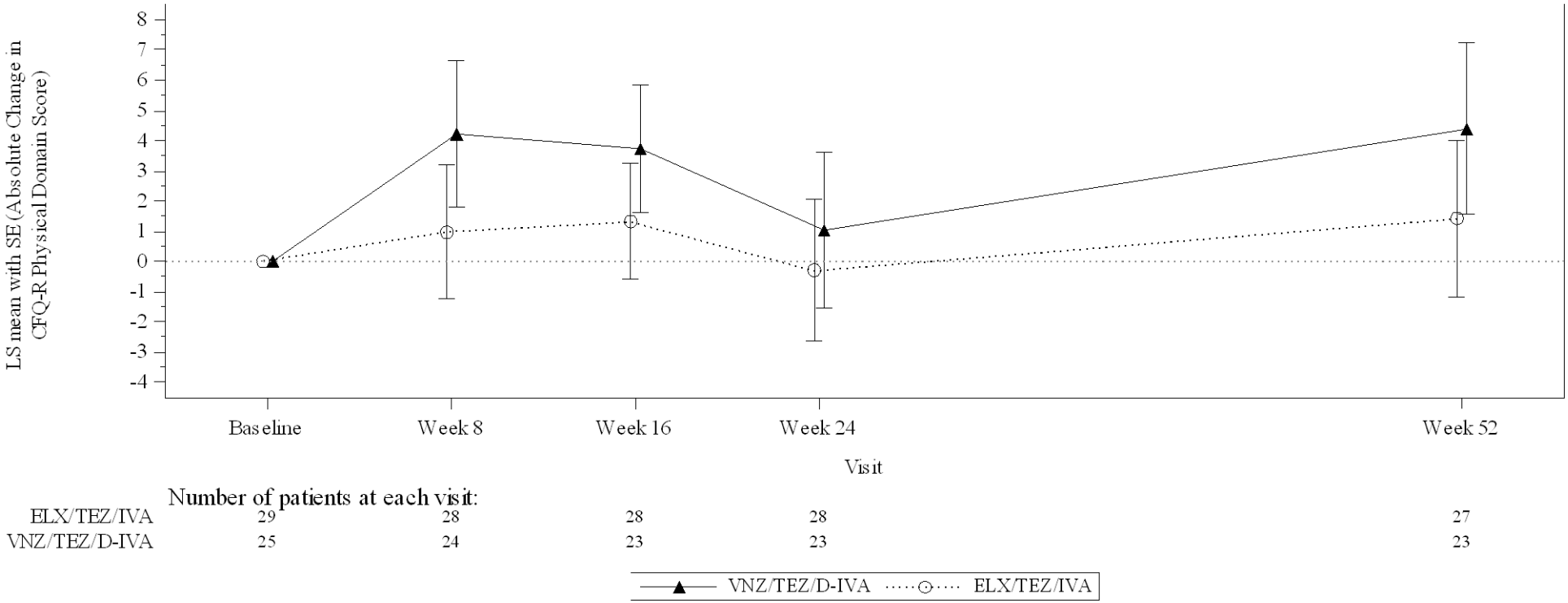
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years



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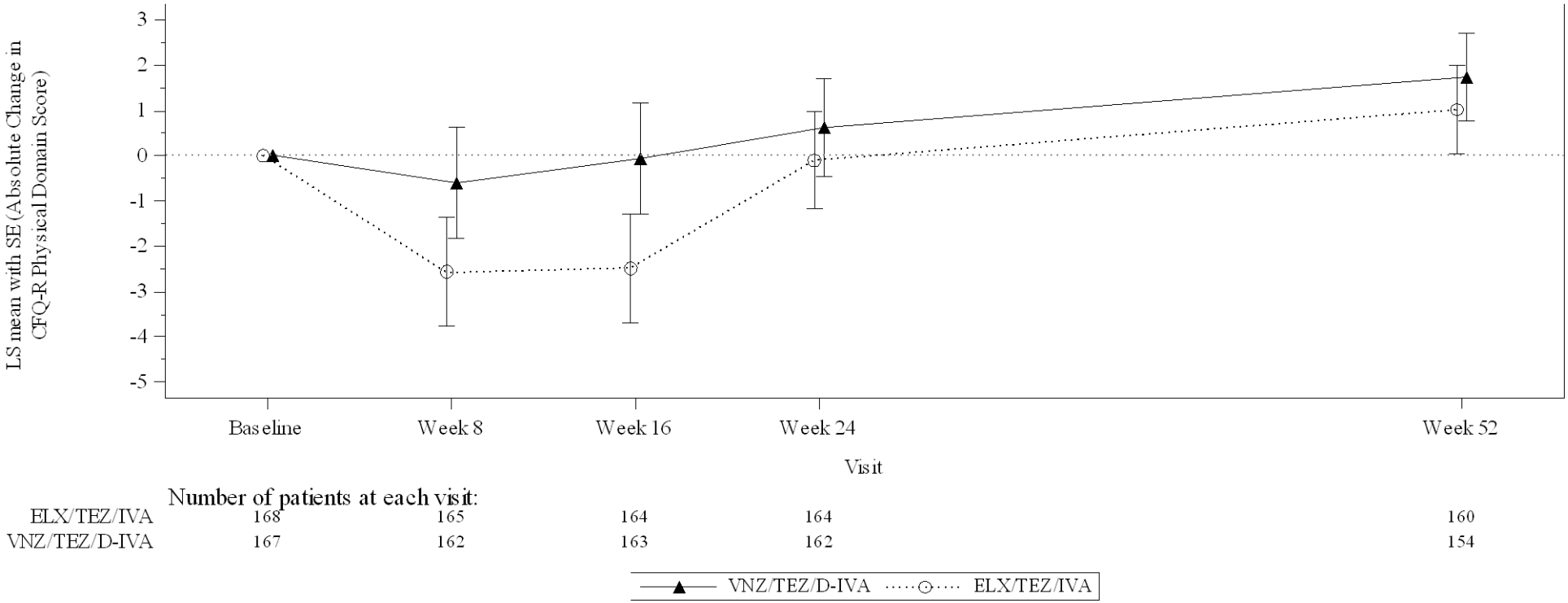
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years



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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

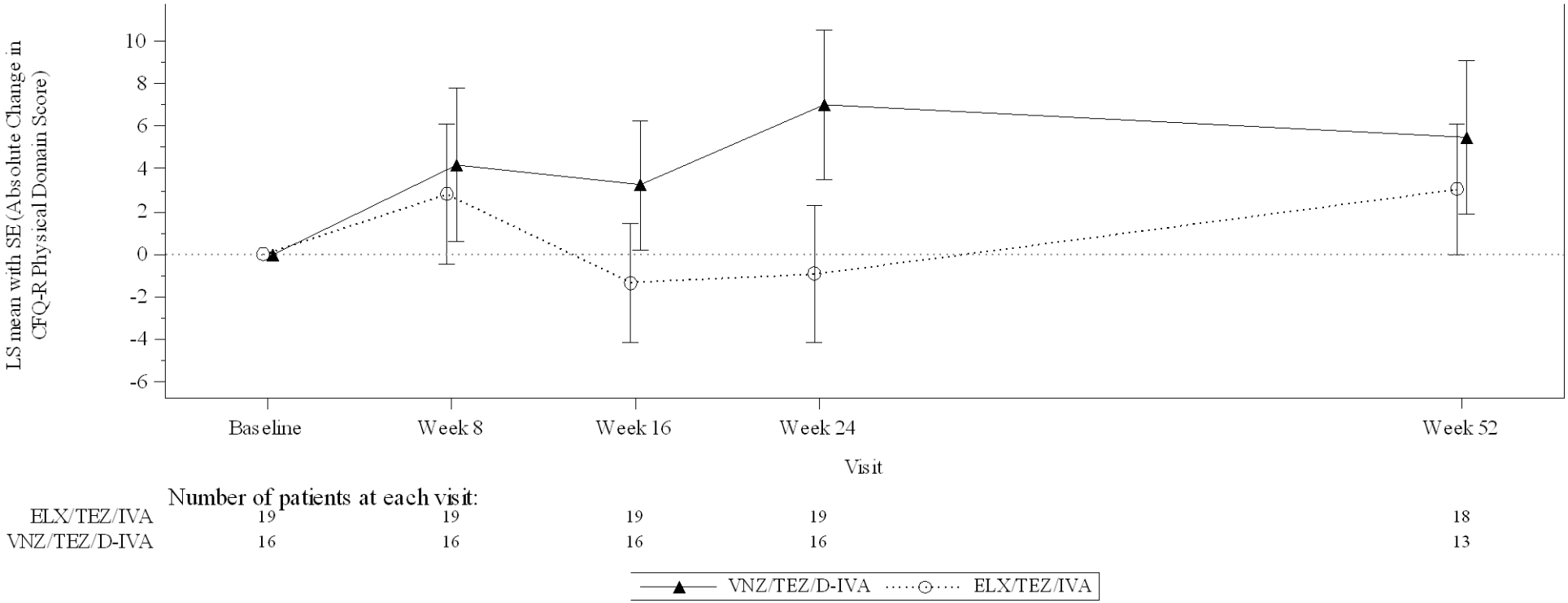

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Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

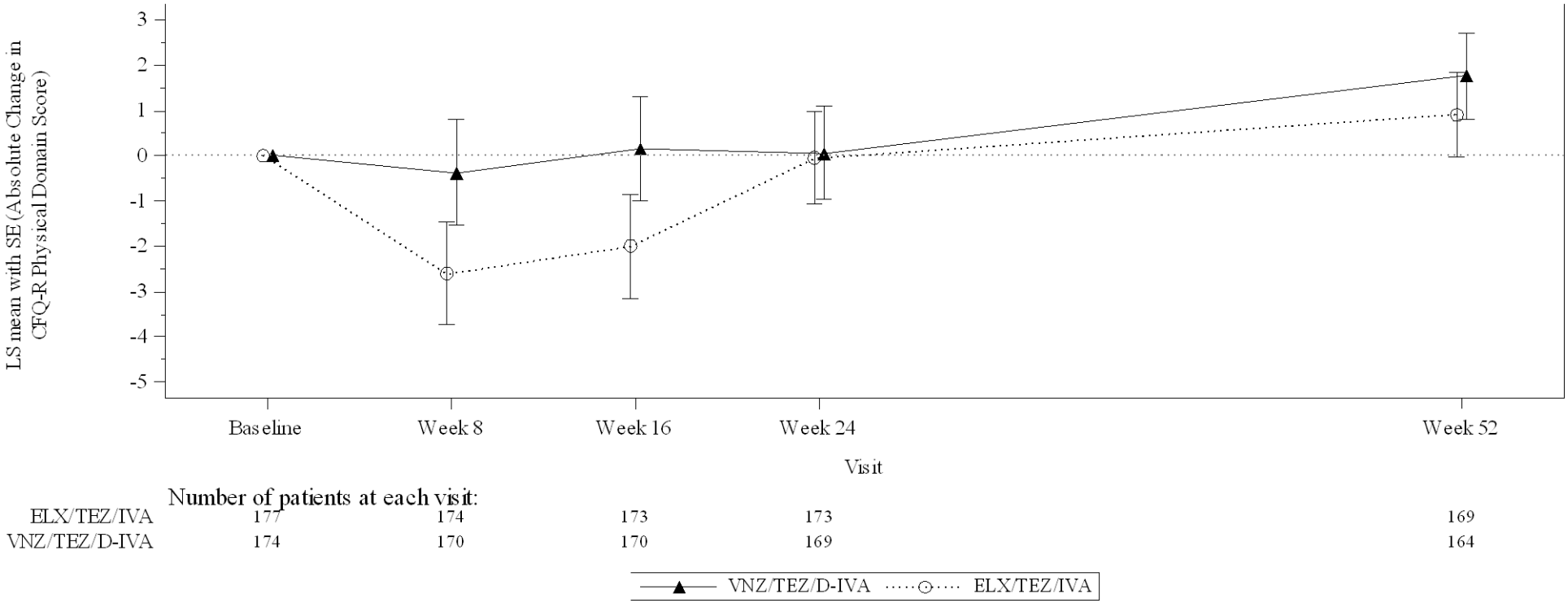

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Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

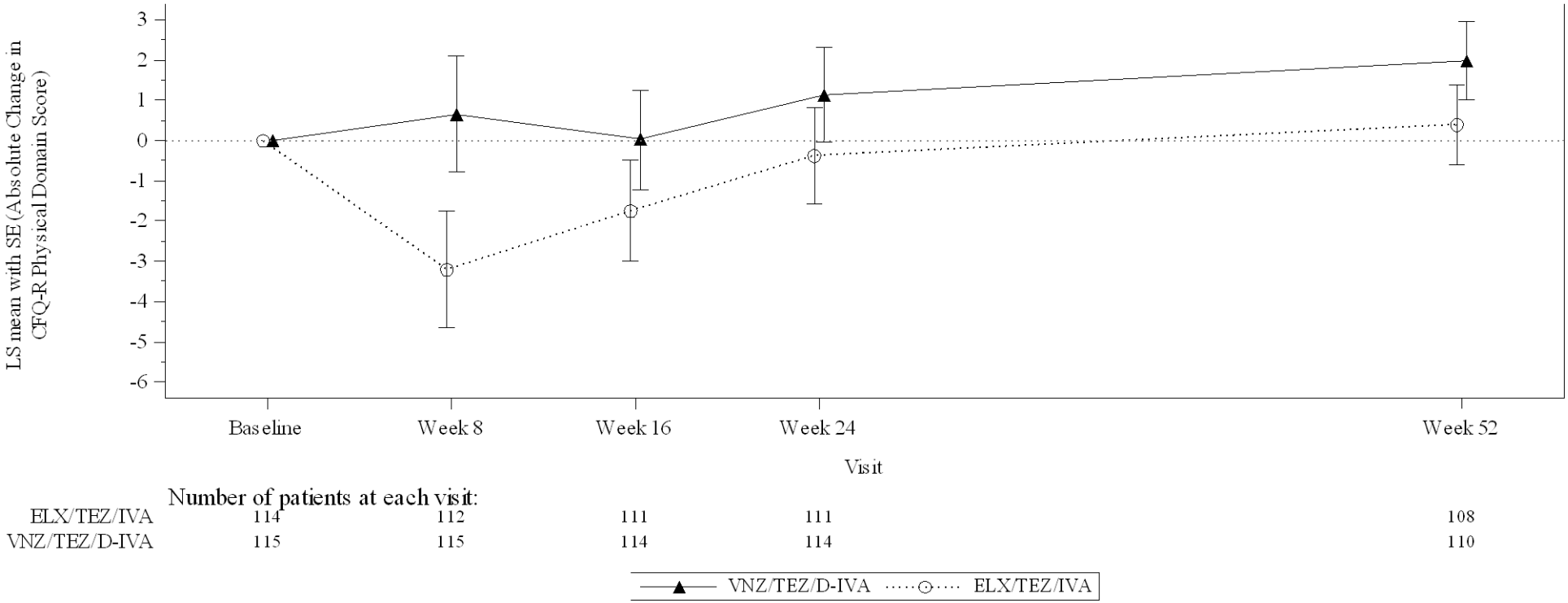

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Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

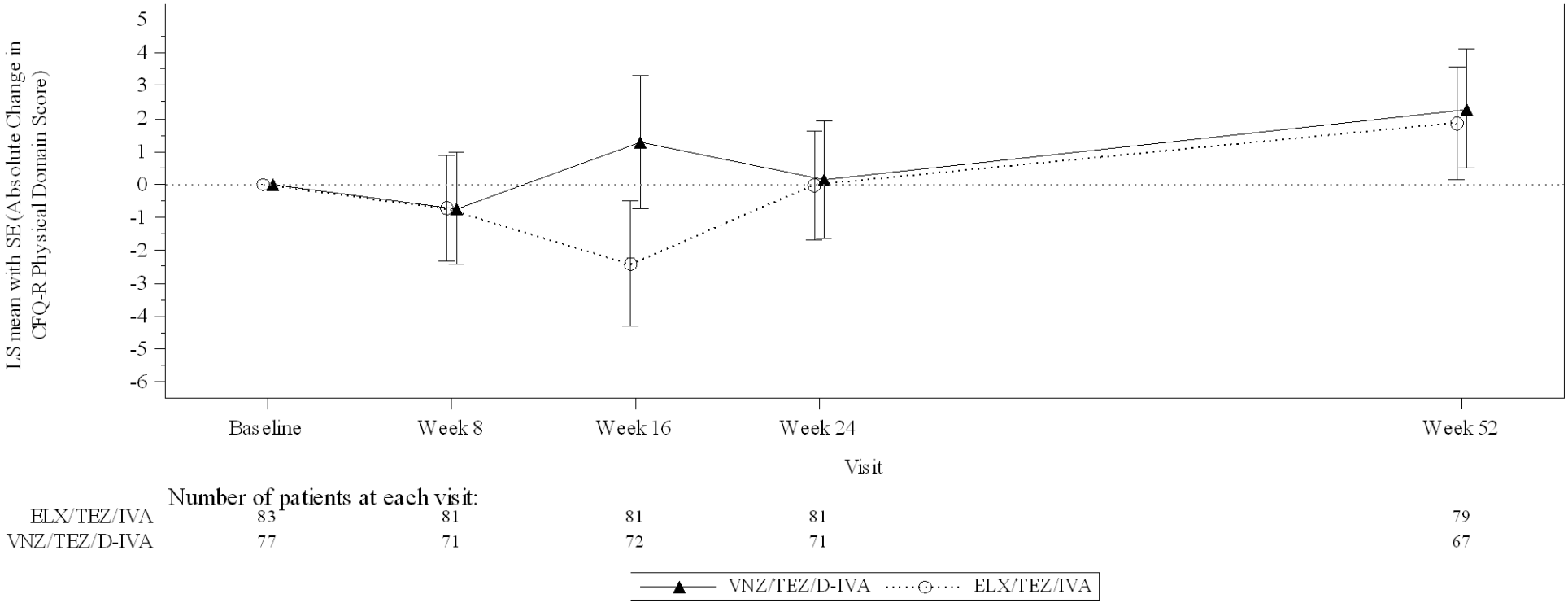

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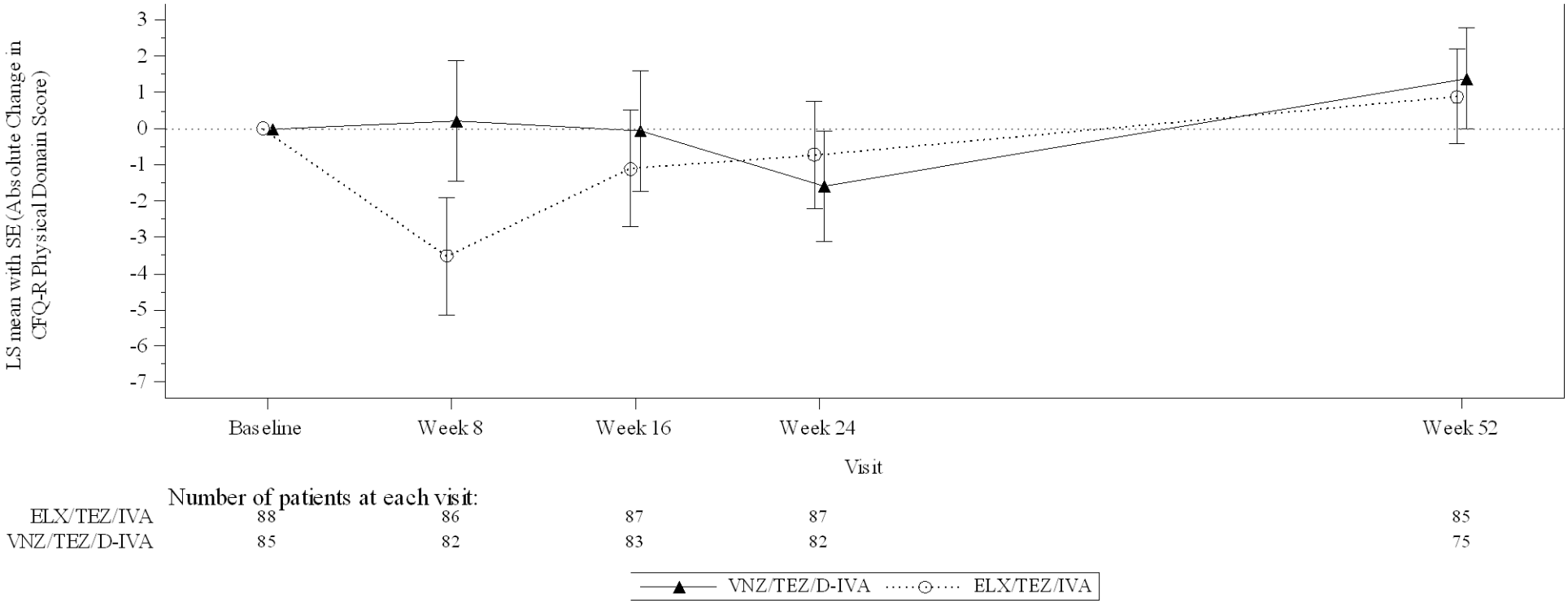
Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America



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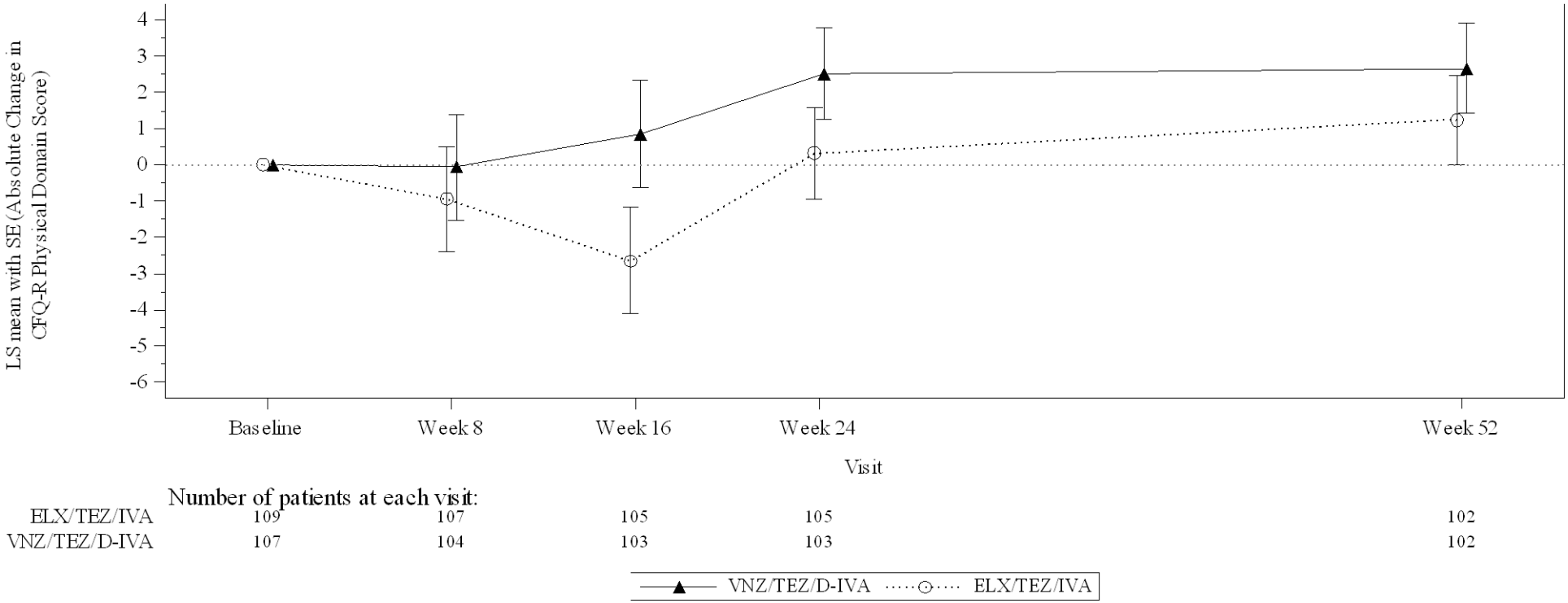
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World



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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
ppFEV$_1$ at baseline <70 %

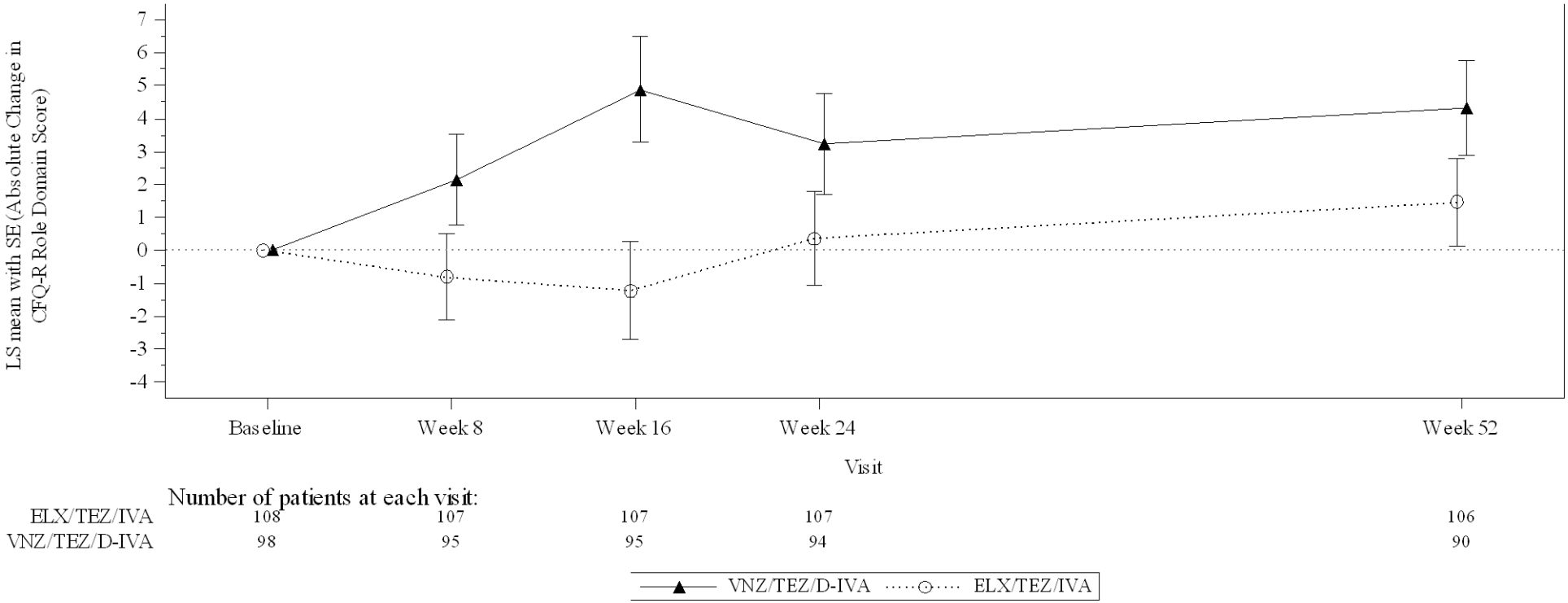

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Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
ppFEV$_1$ at baseline ≥70 %

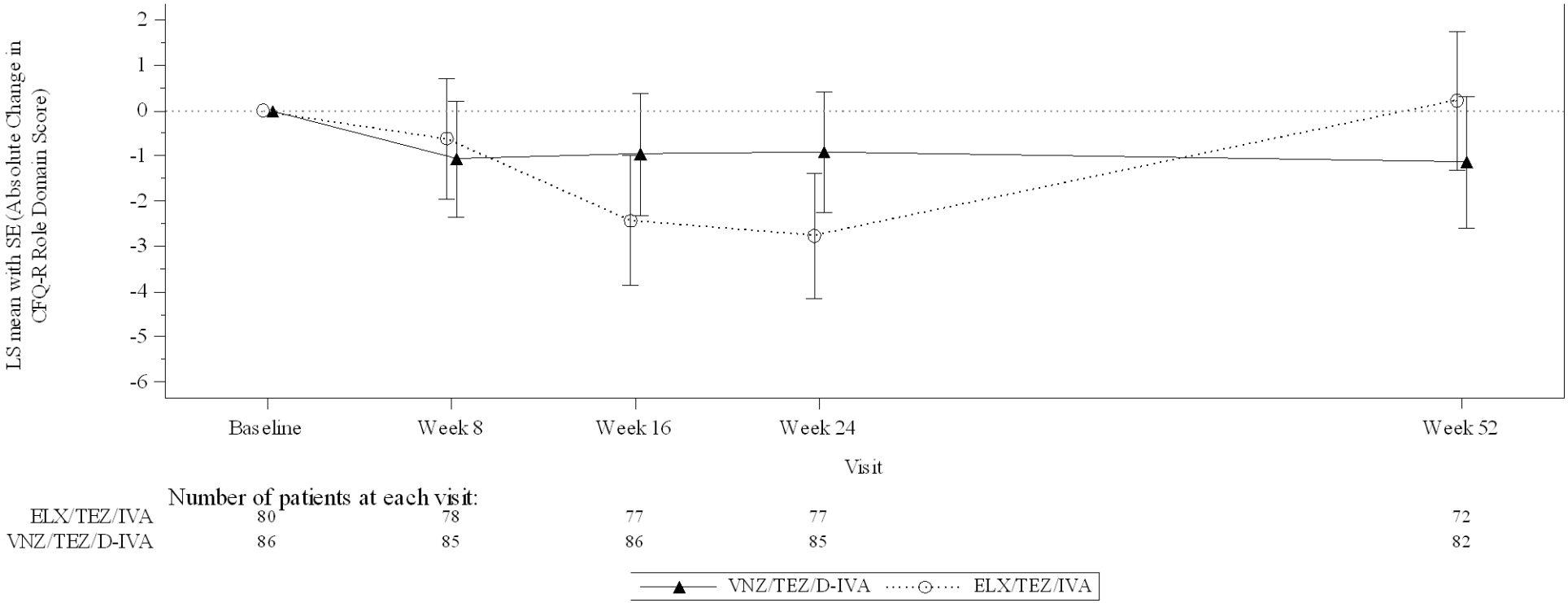

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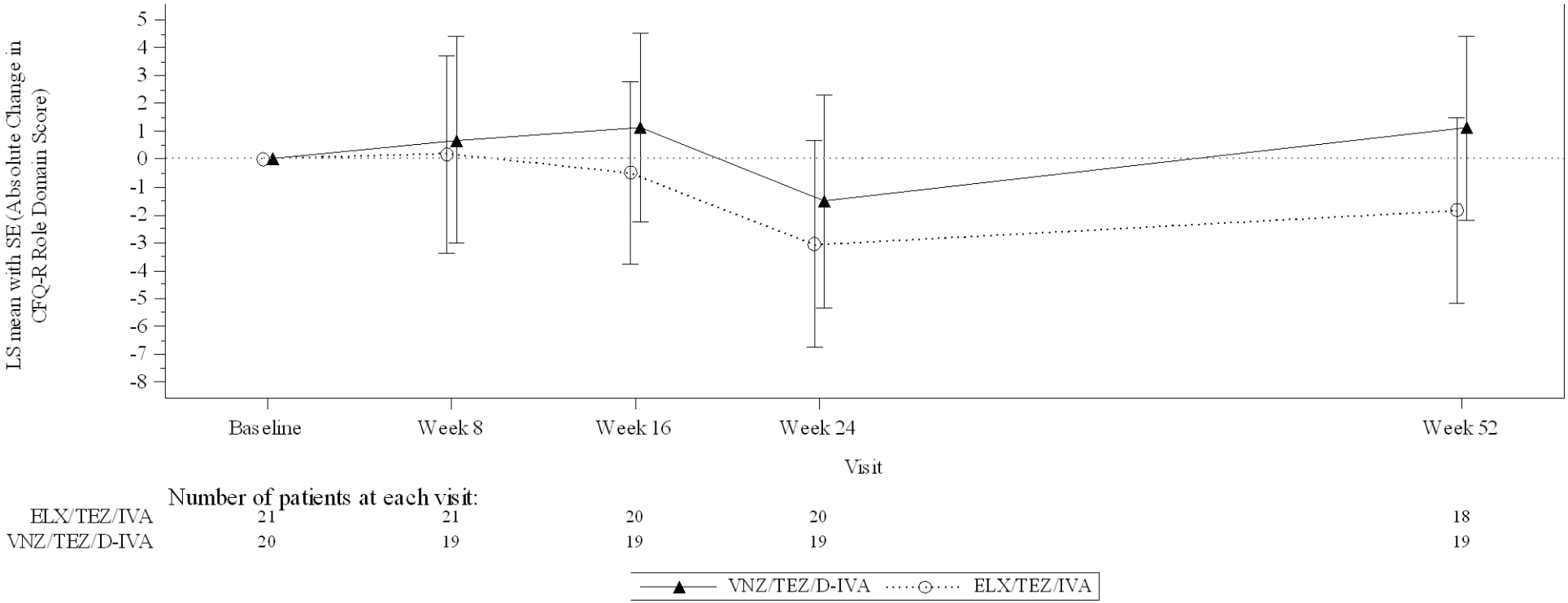
Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years



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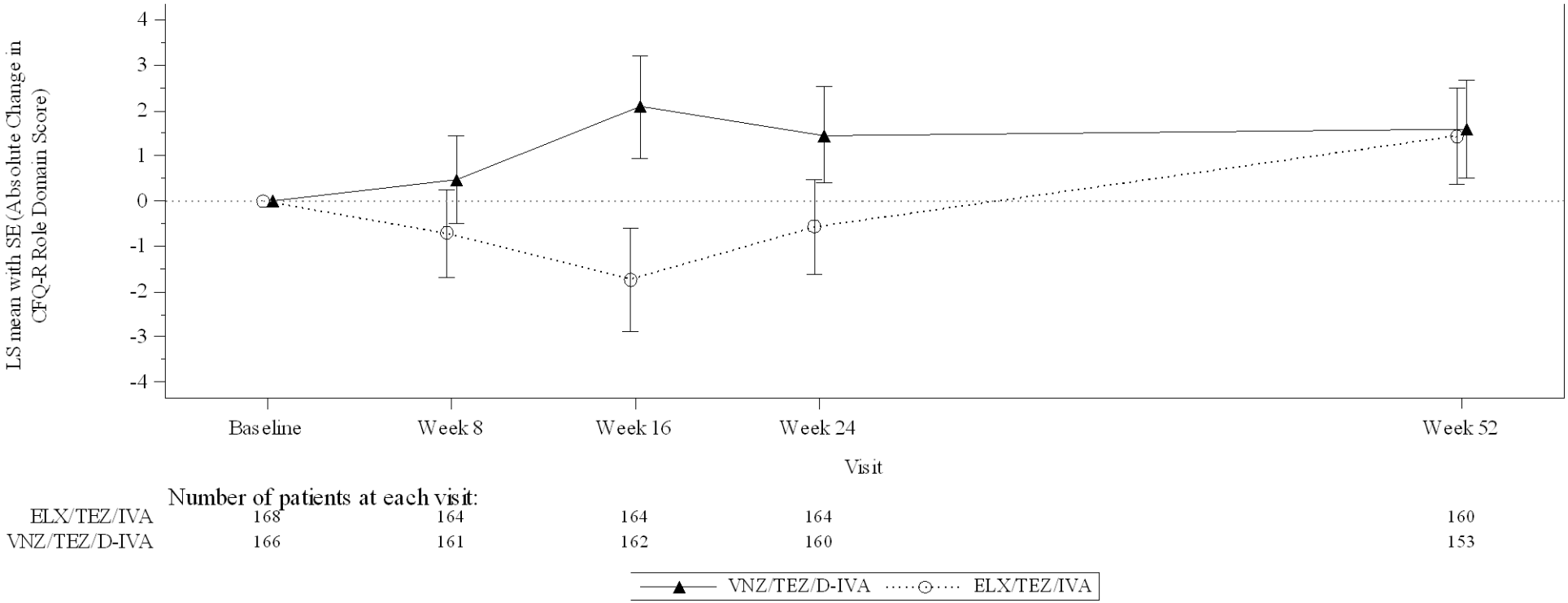
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years



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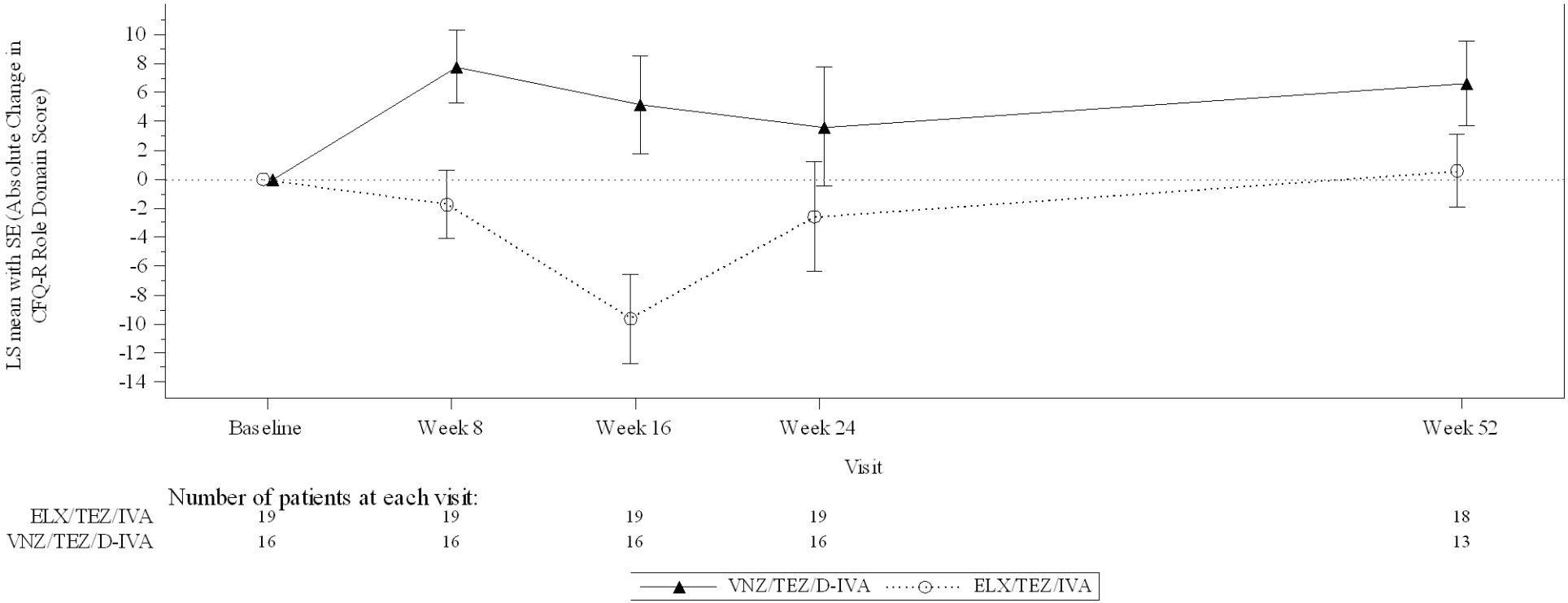
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L



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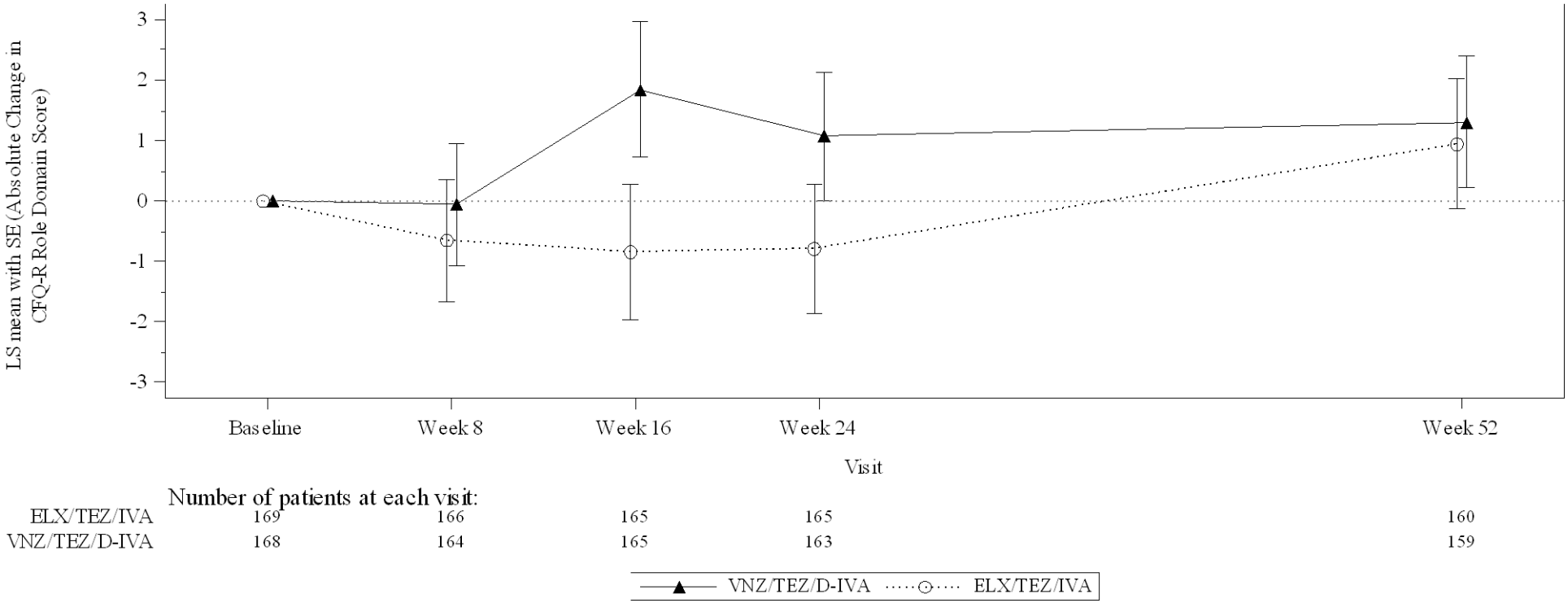
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L



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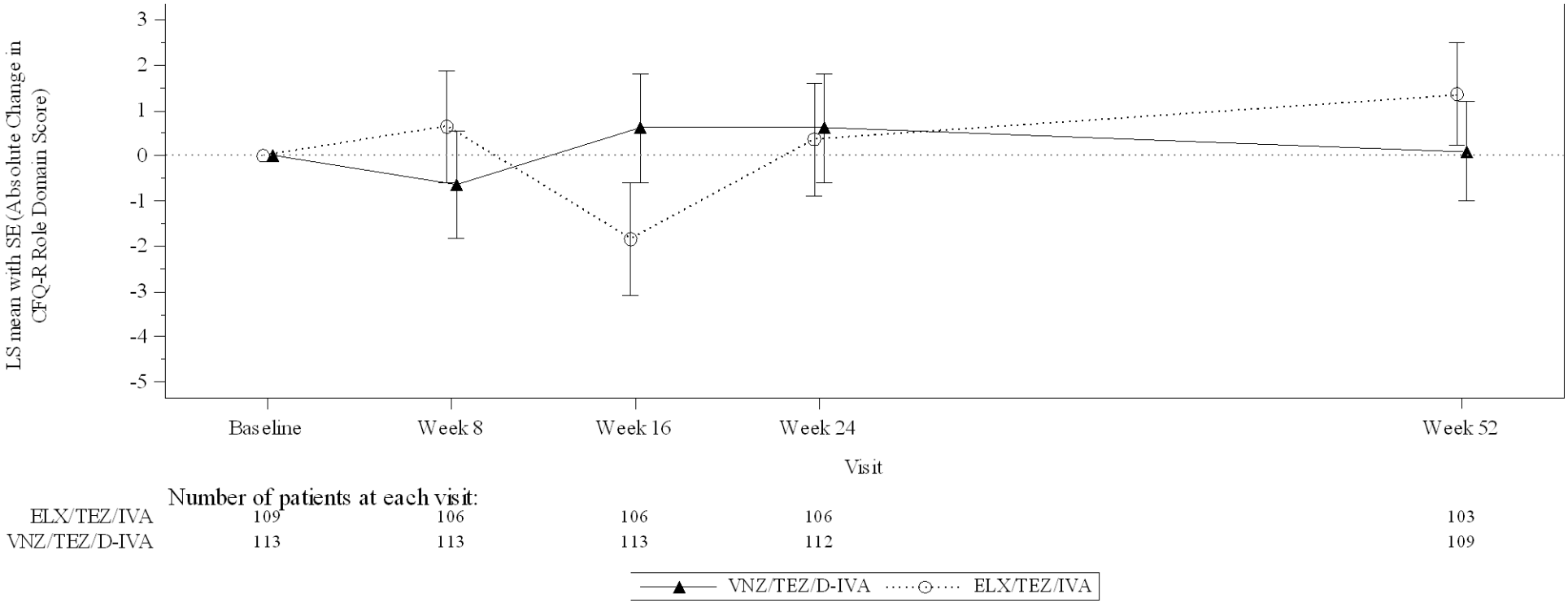
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Male



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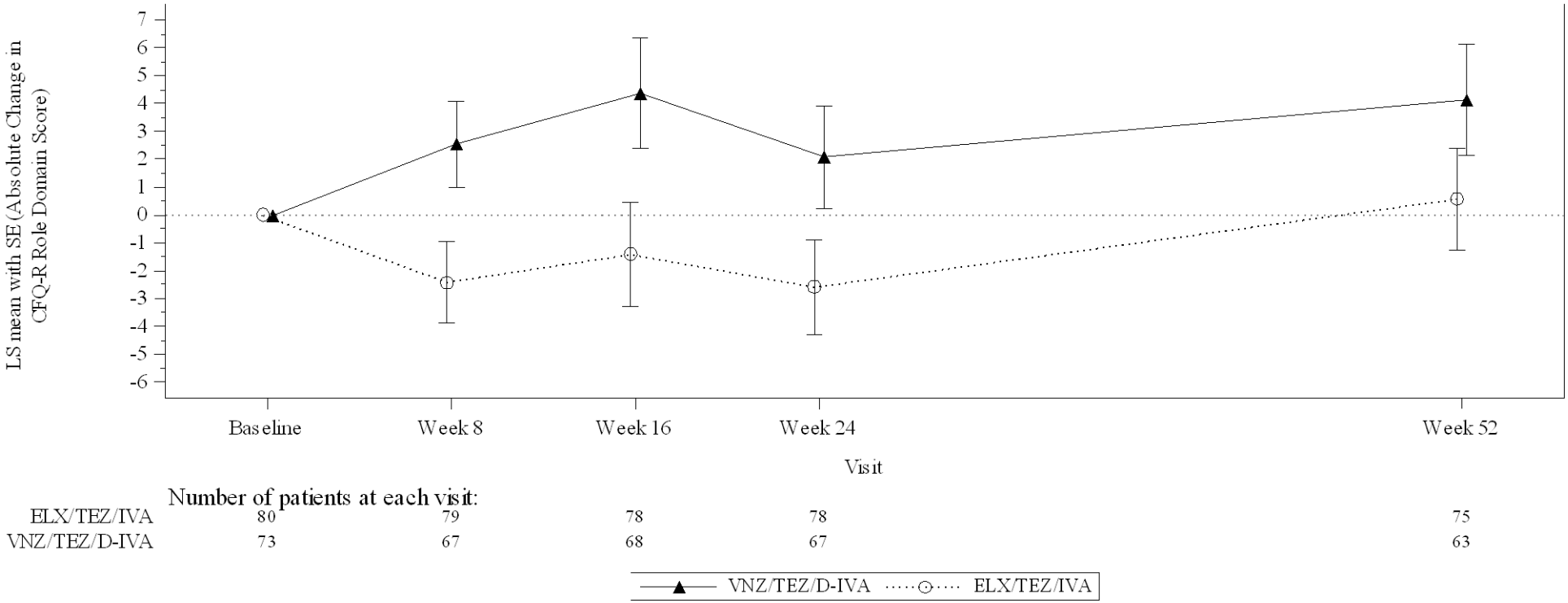
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Female



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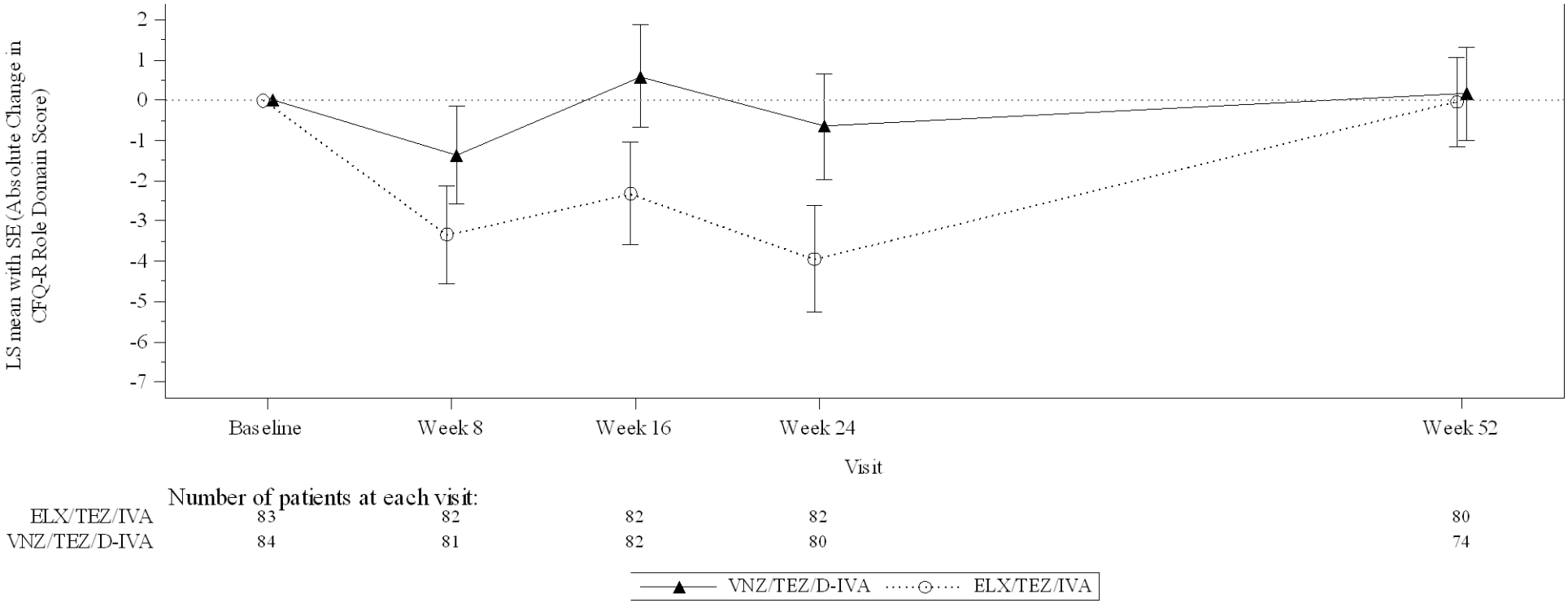
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = North America



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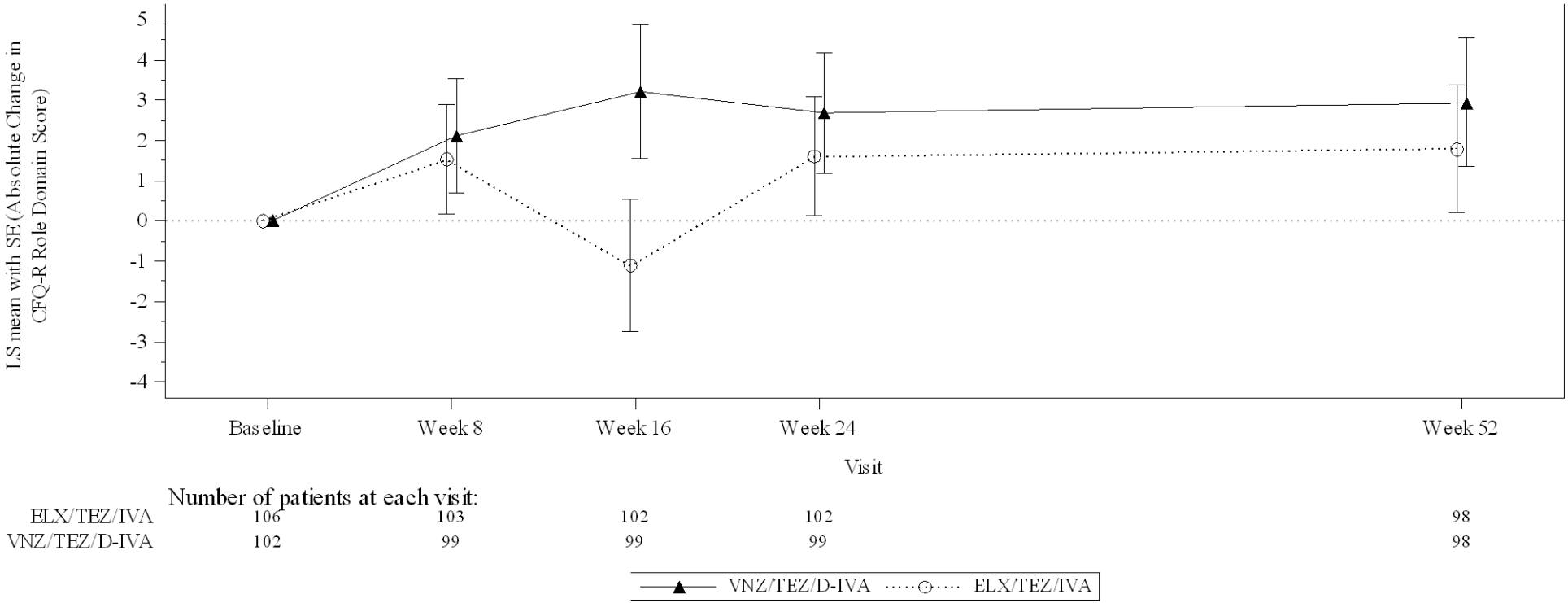
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World



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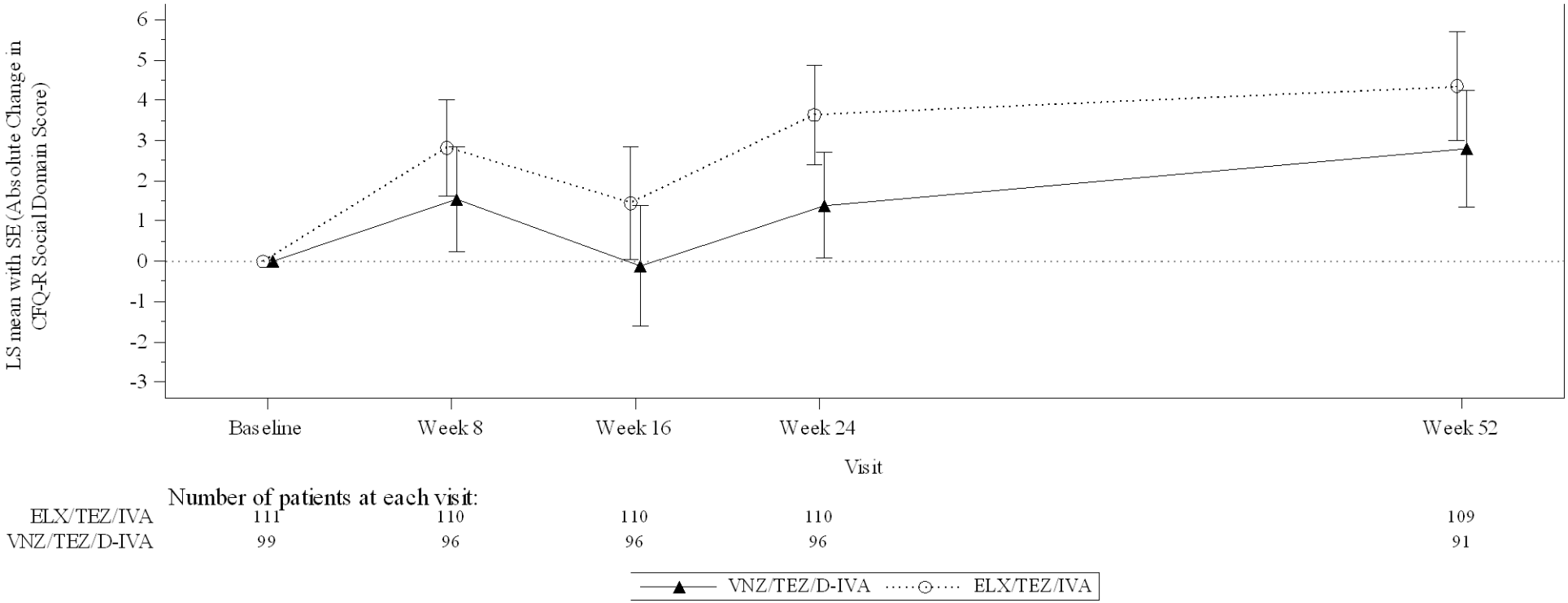
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
ppFEV$_1$ at baseline <70 %



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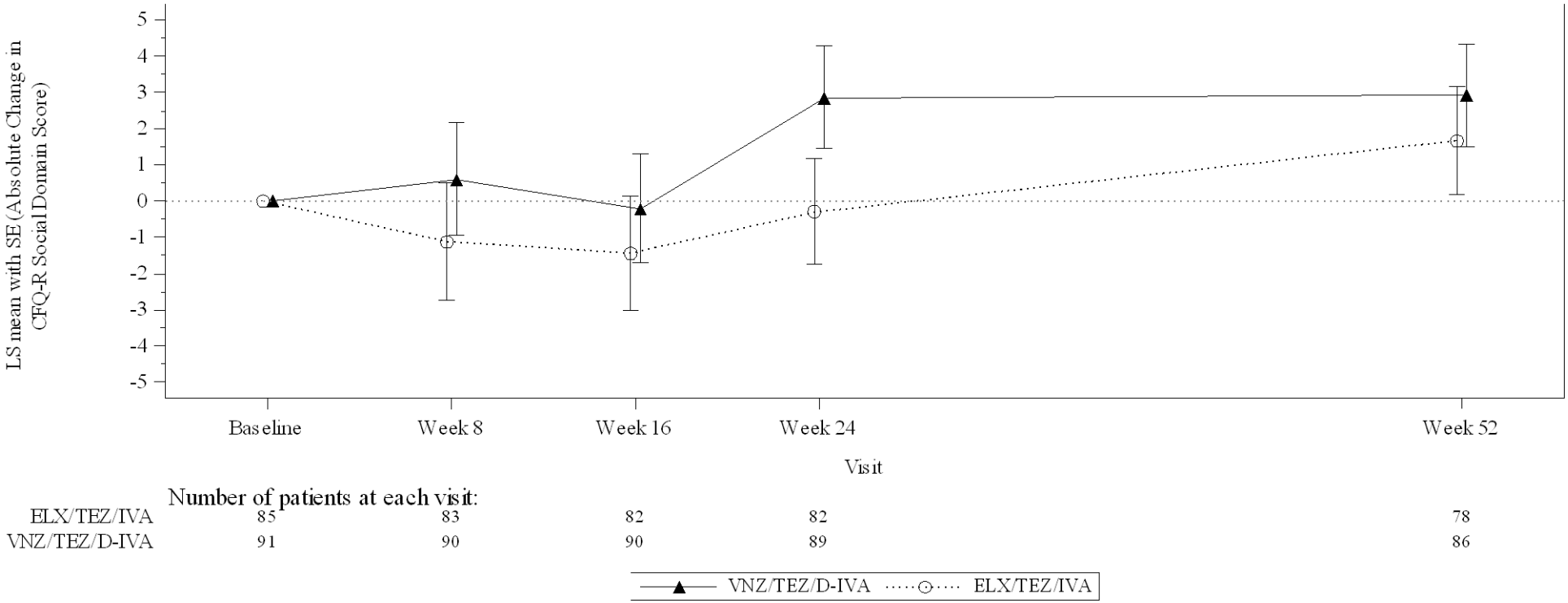
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
ppFEV$_1$ at baseline ≥70 %



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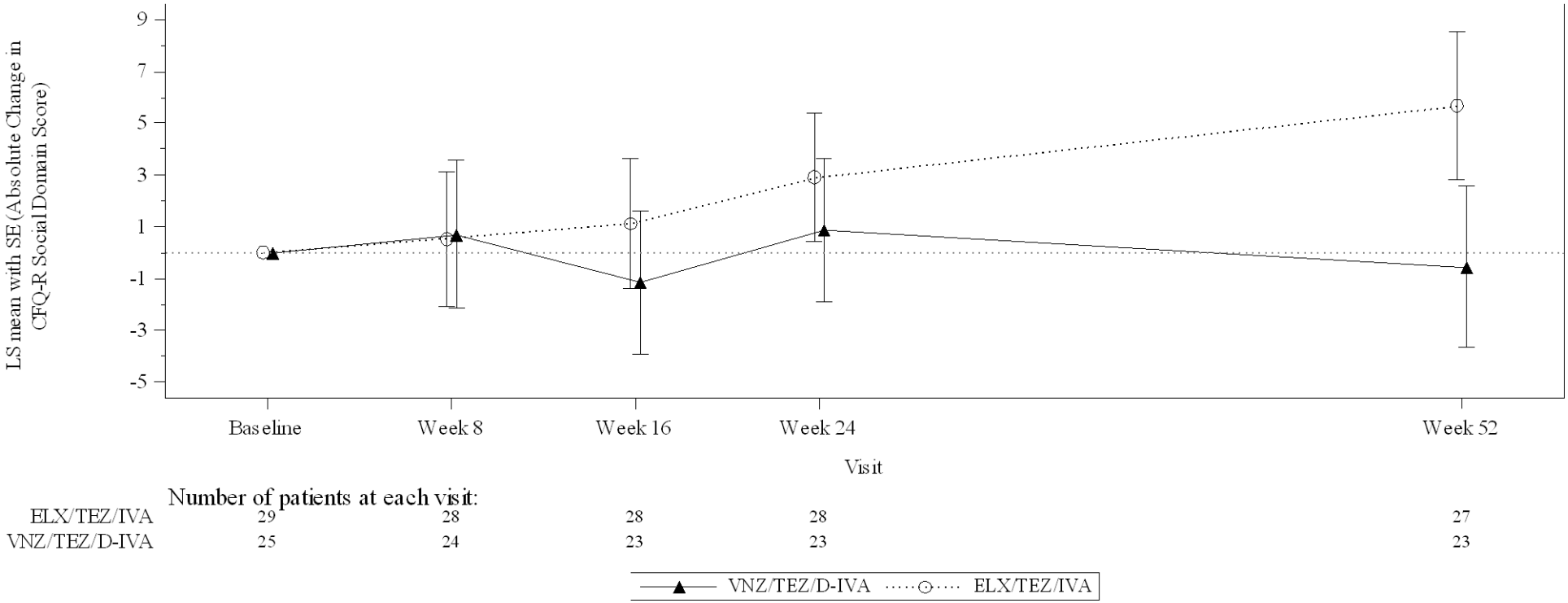
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years



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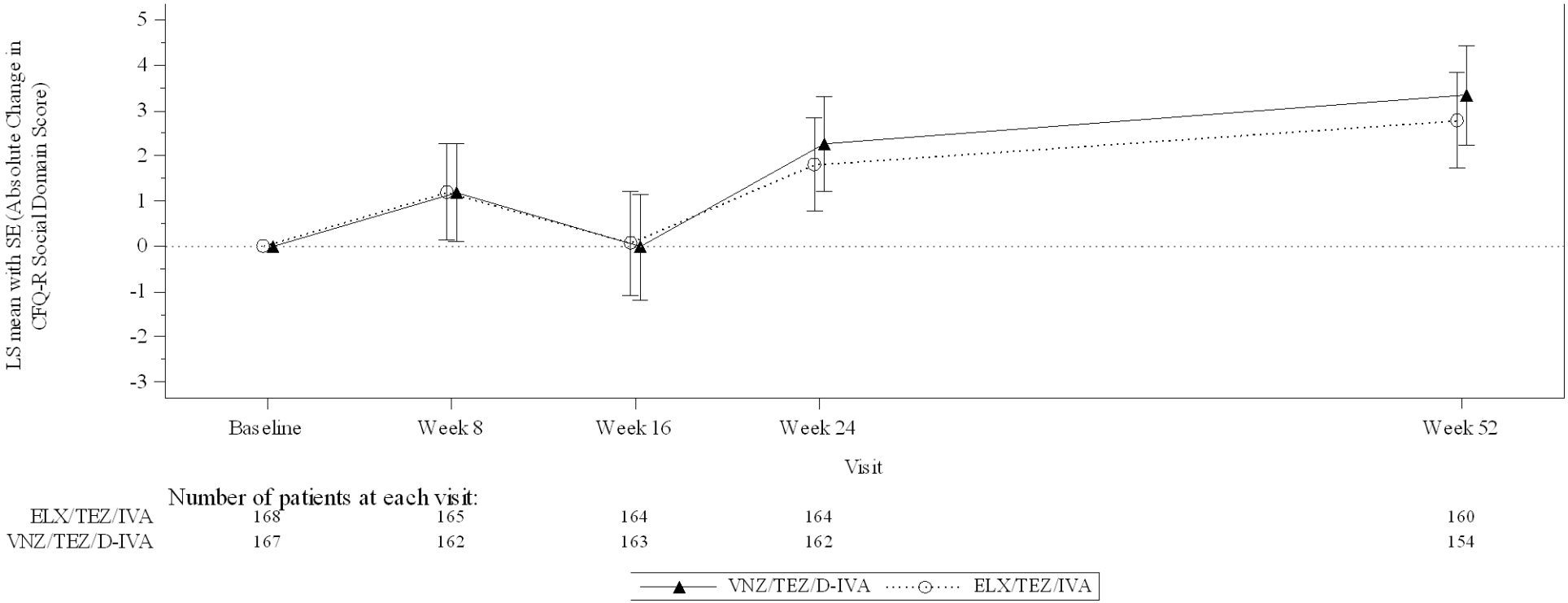
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years



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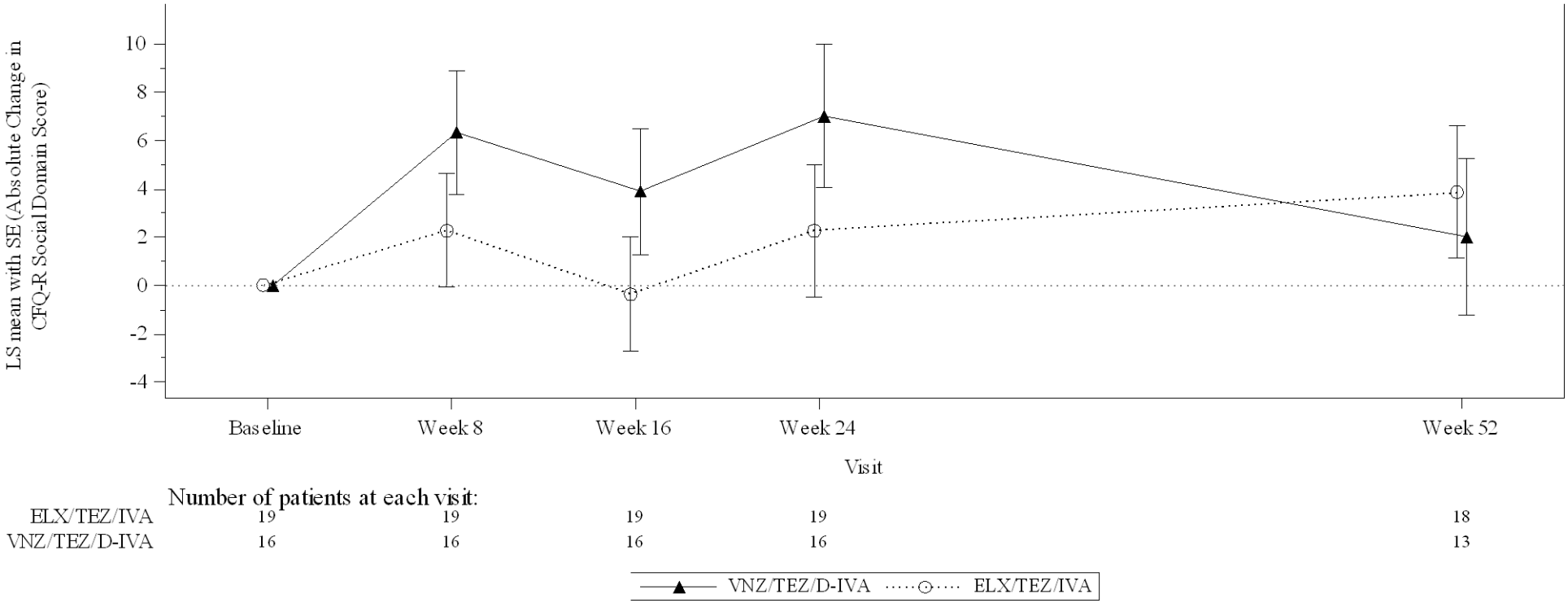
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L



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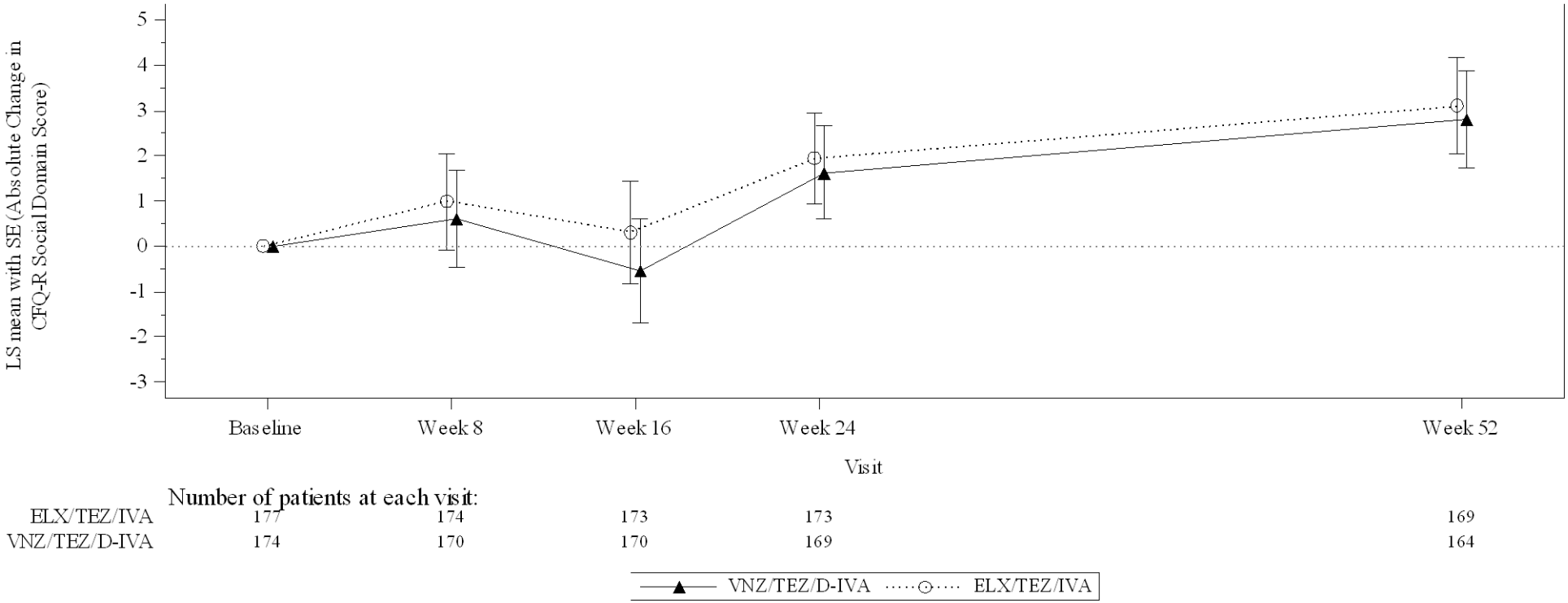
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L



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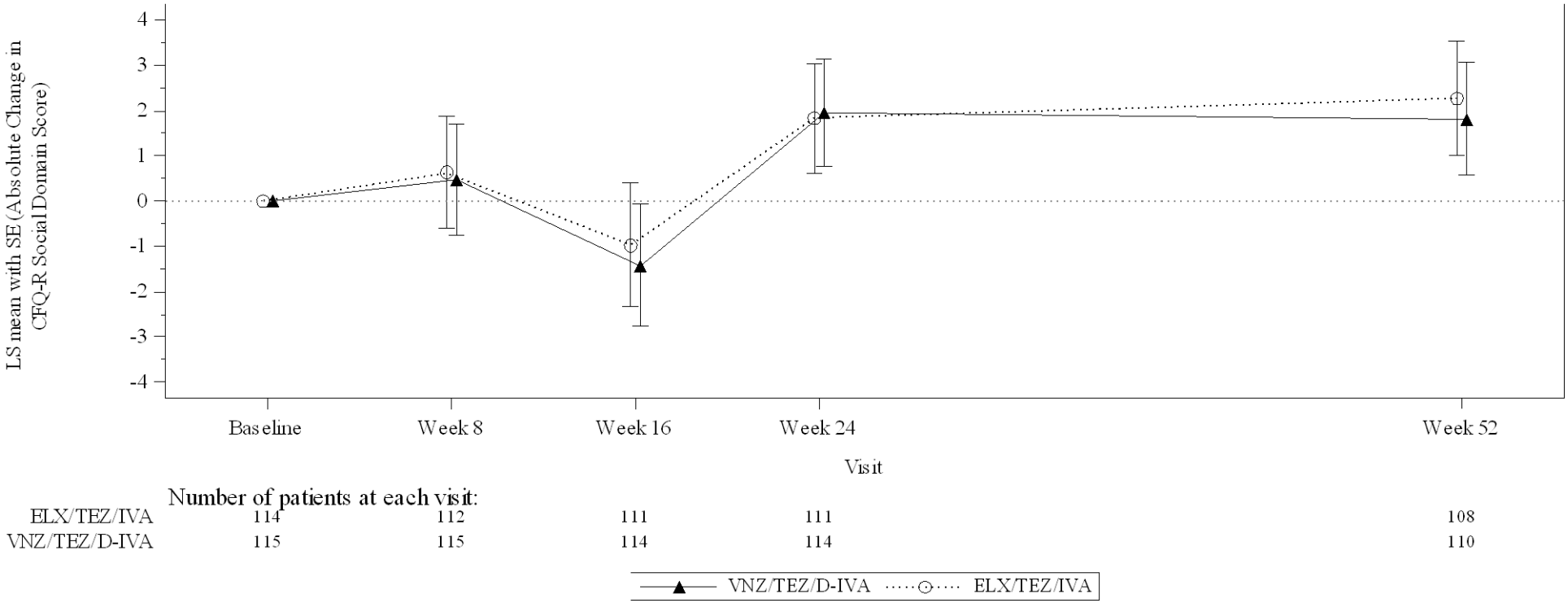
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male



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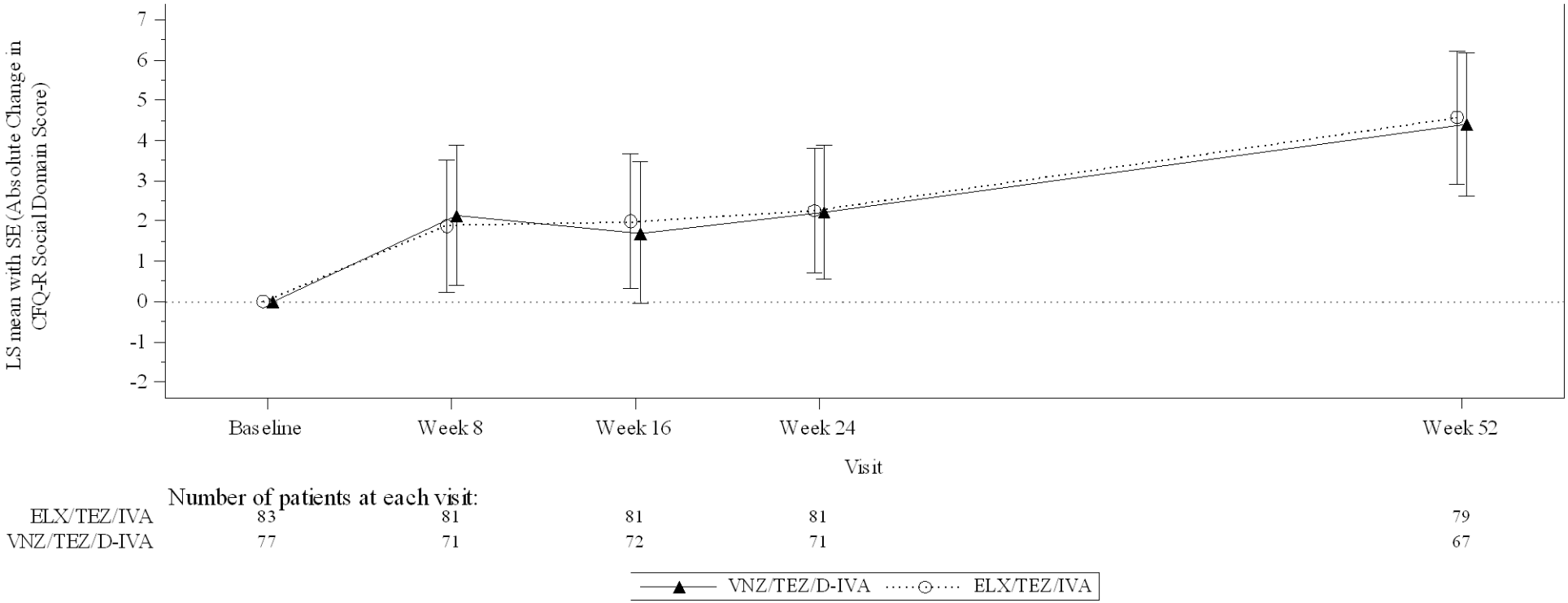
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female



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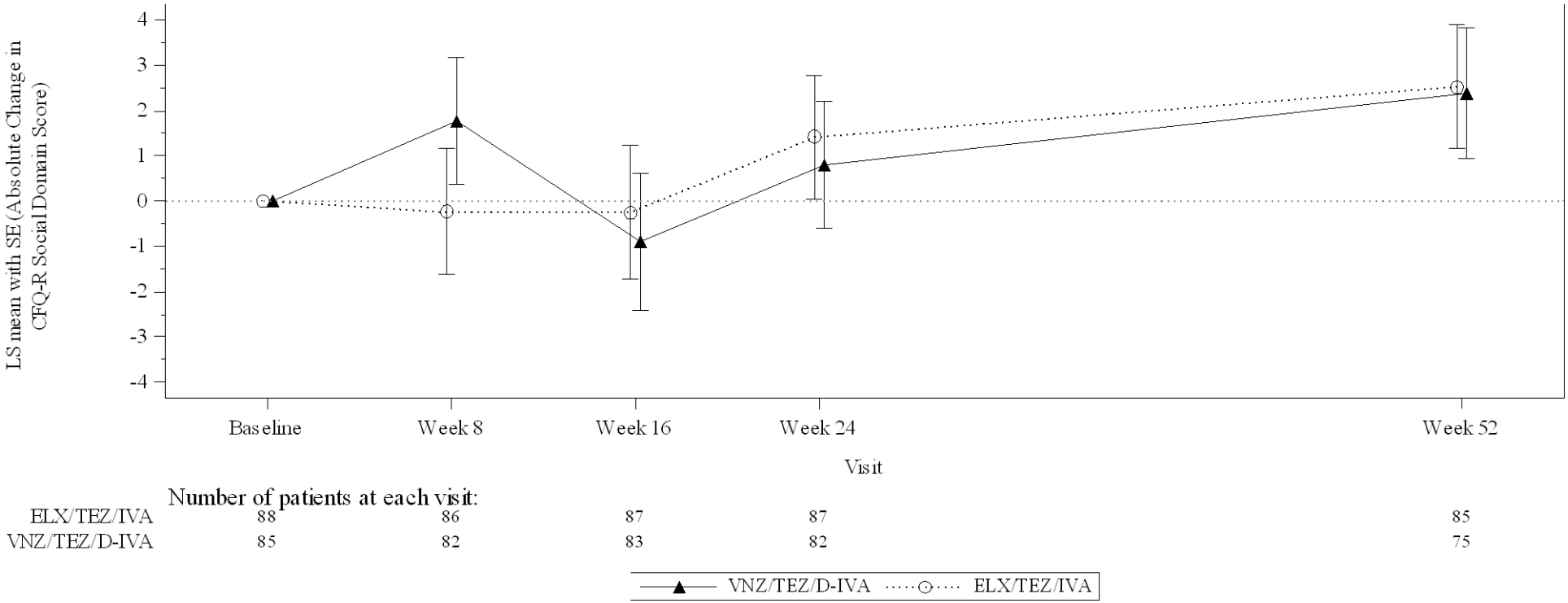
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America



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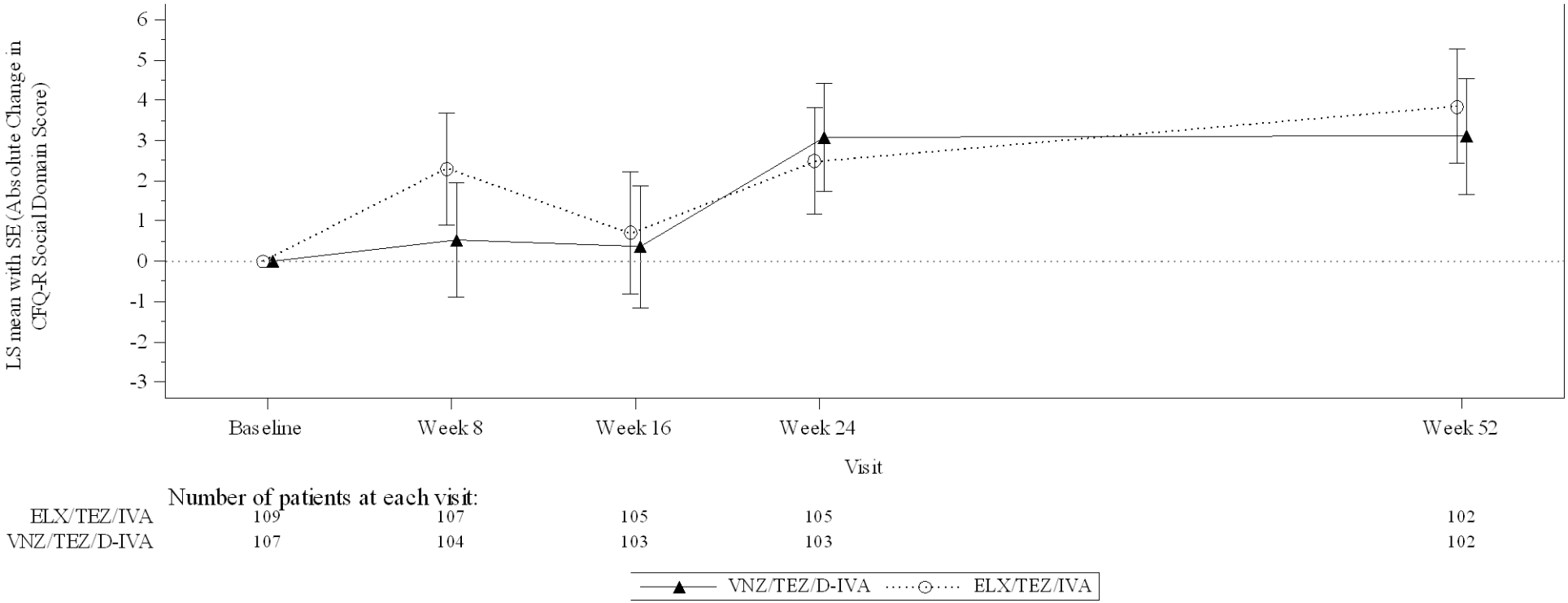
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World



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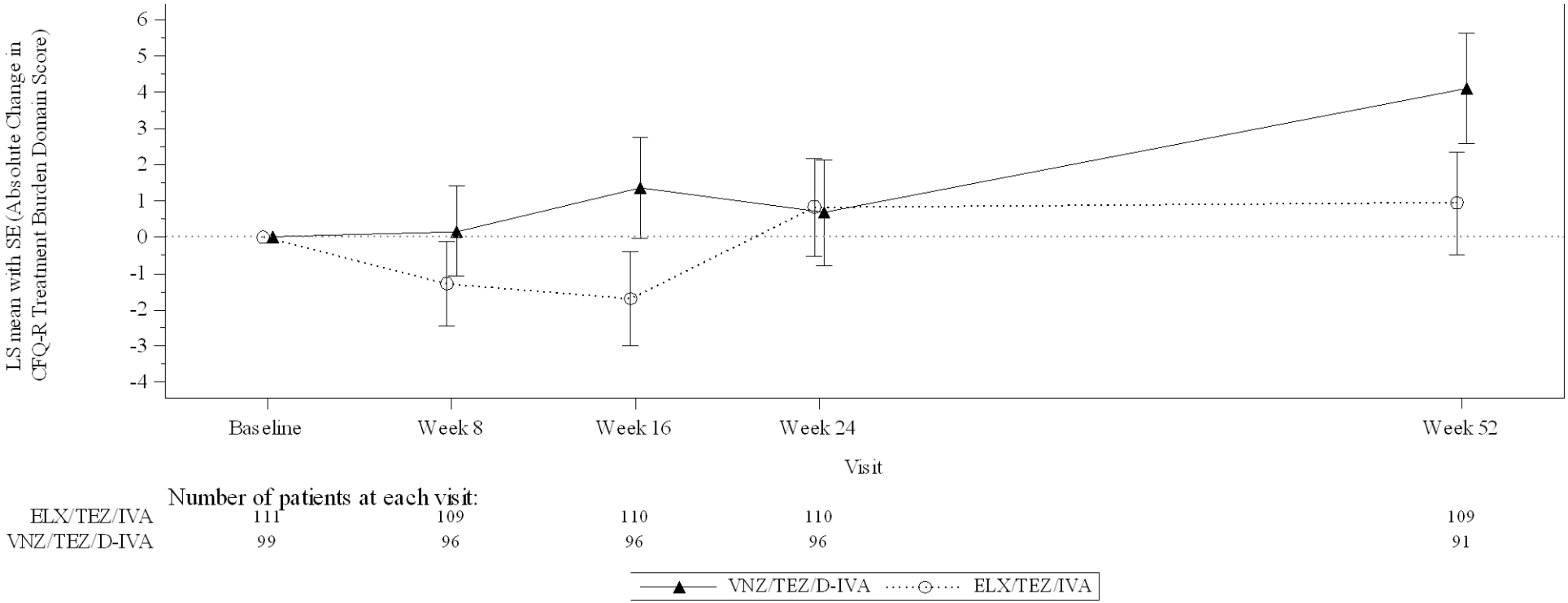
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
ppFEV$_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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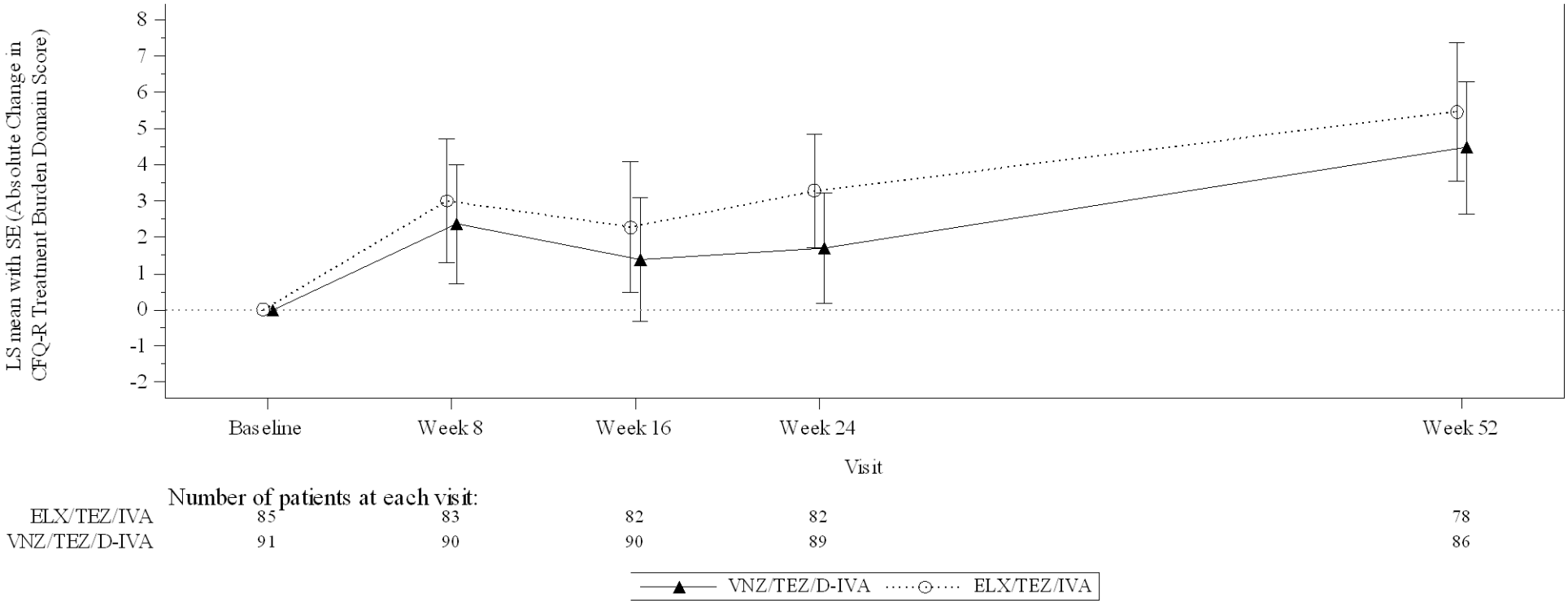
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
ppFEV$_1$ at baseline ≥70 %



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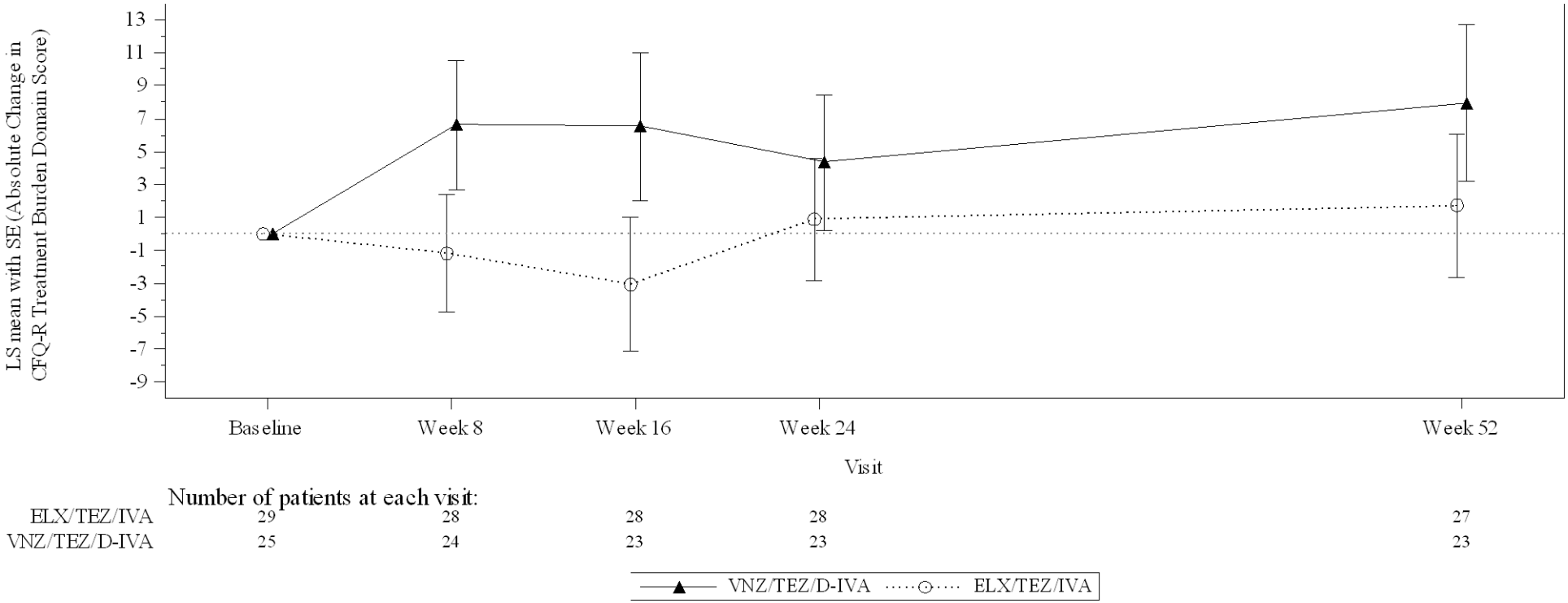
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years



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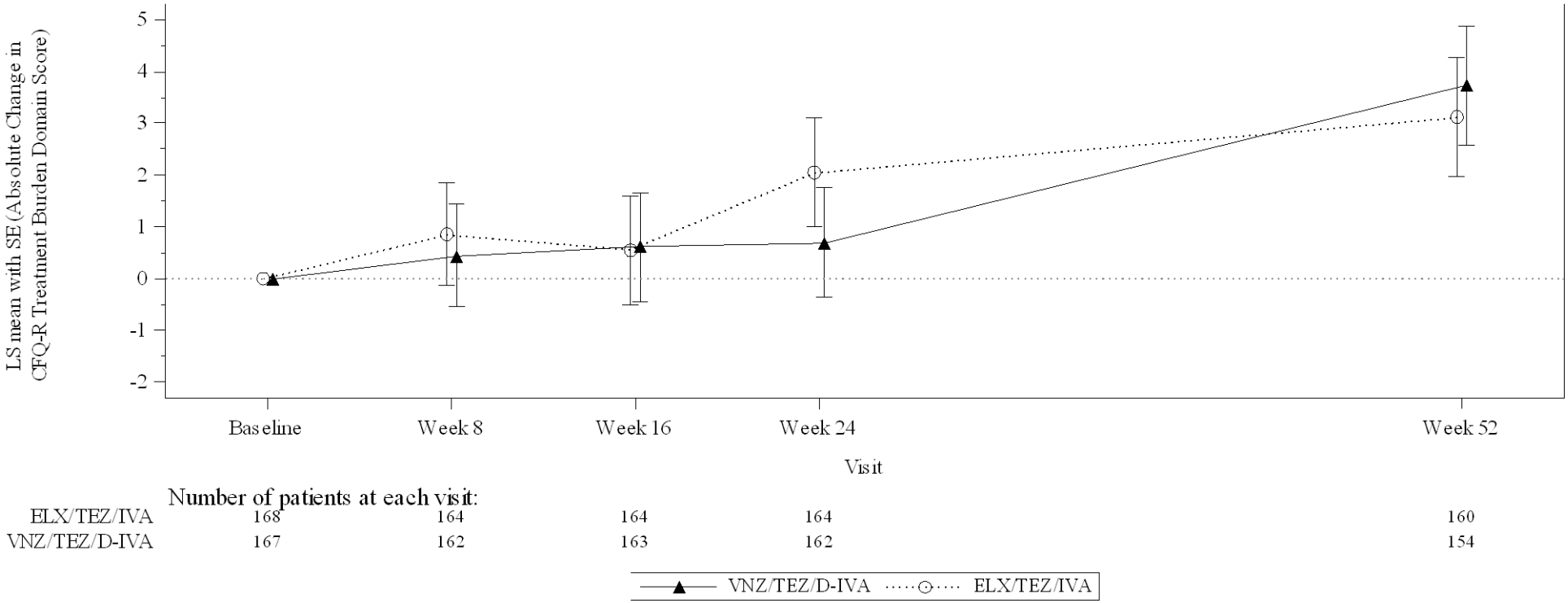
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years



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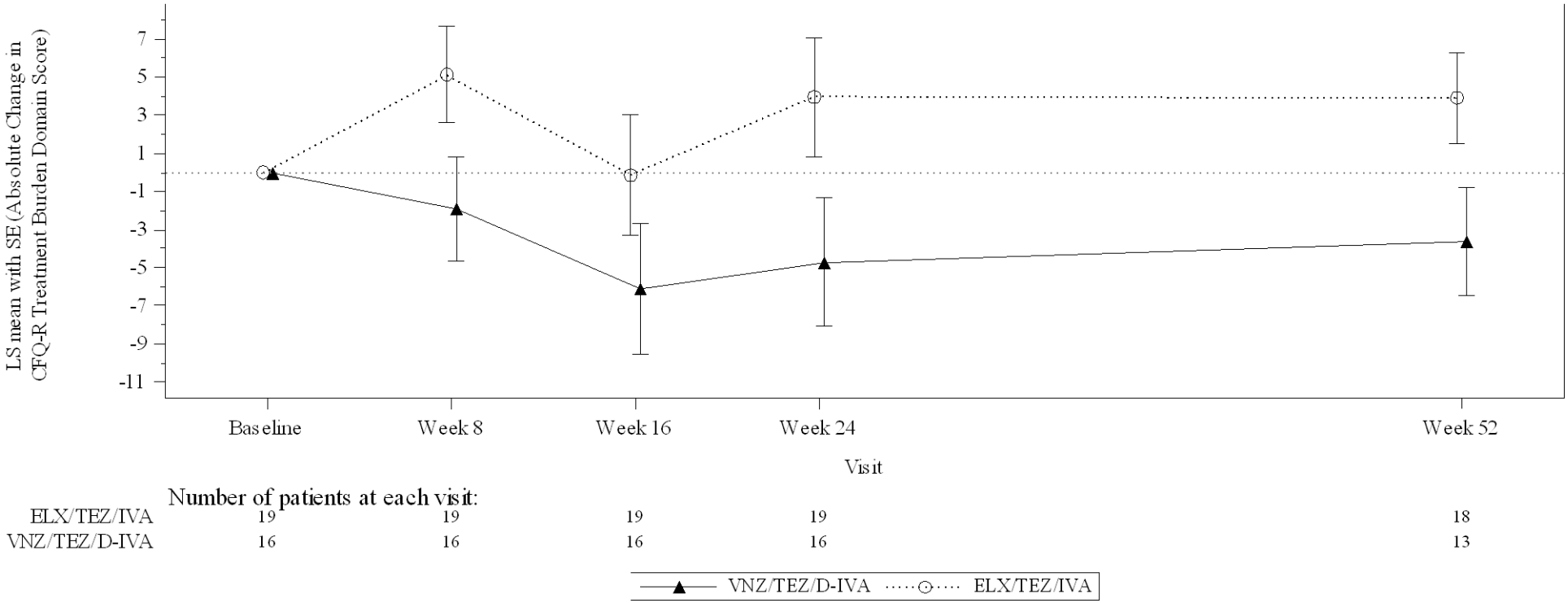
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L



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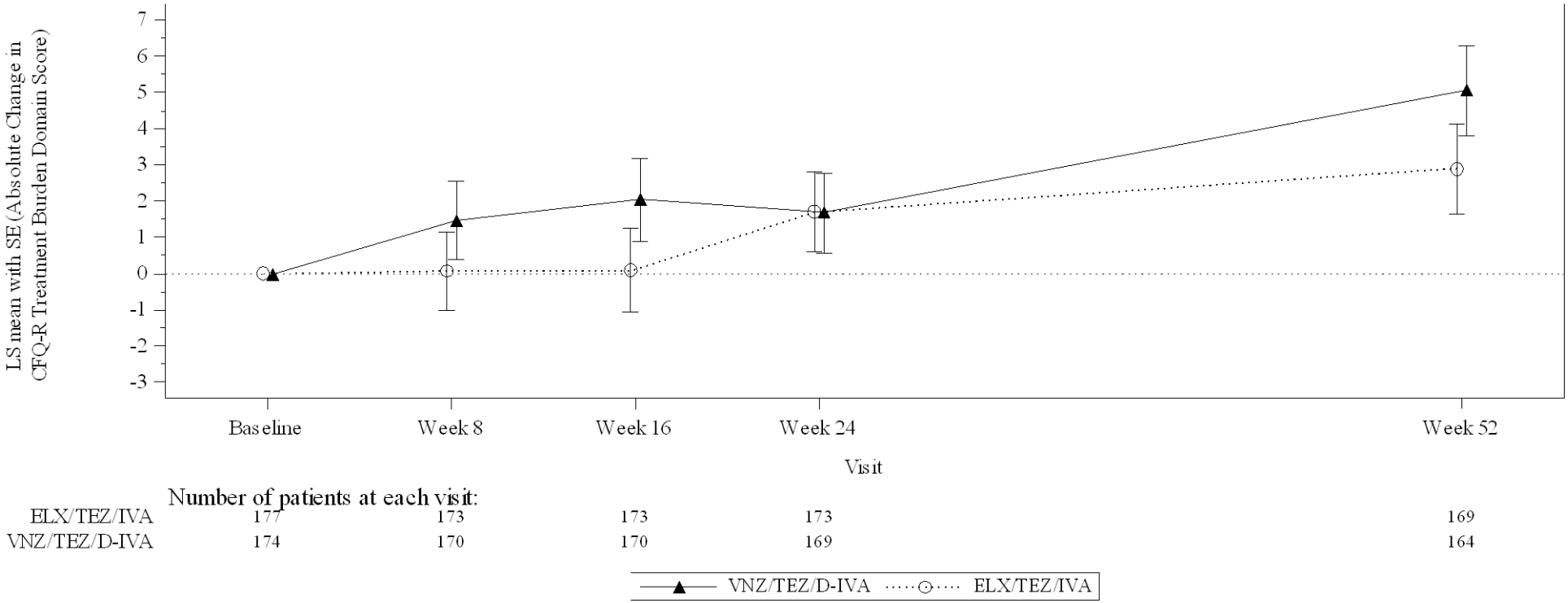
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L



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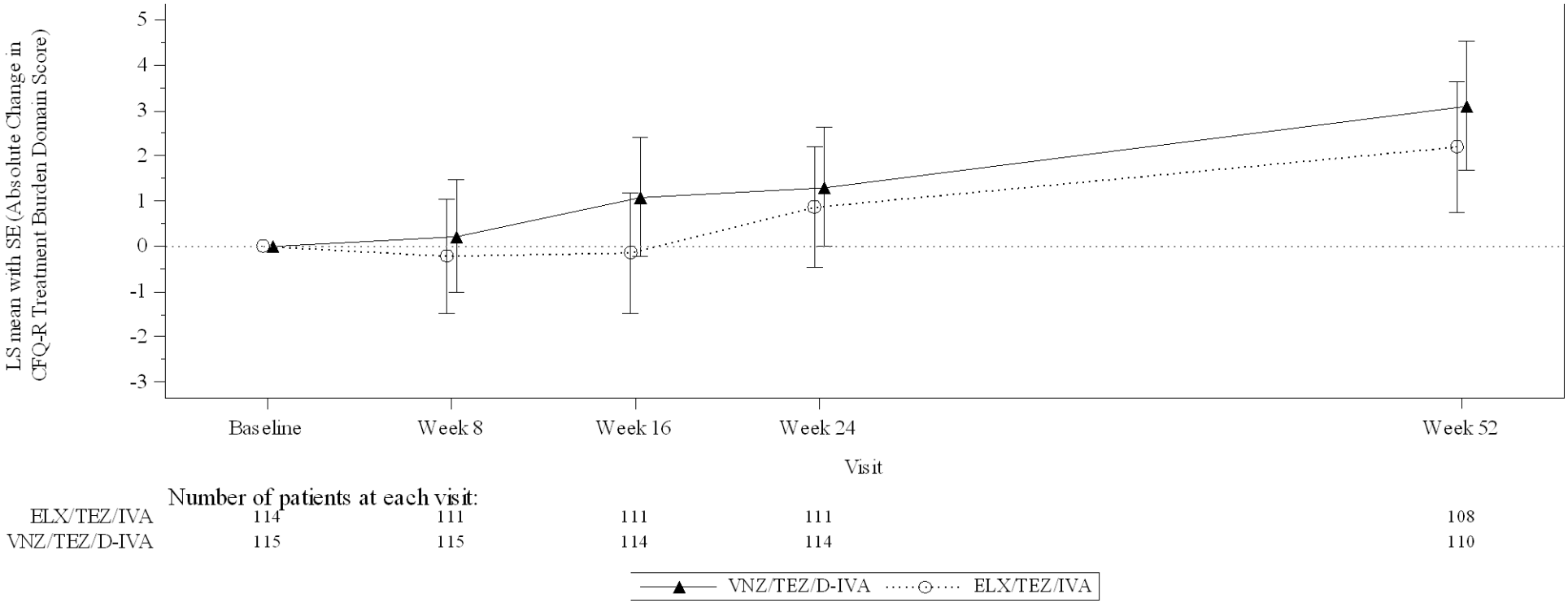
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male



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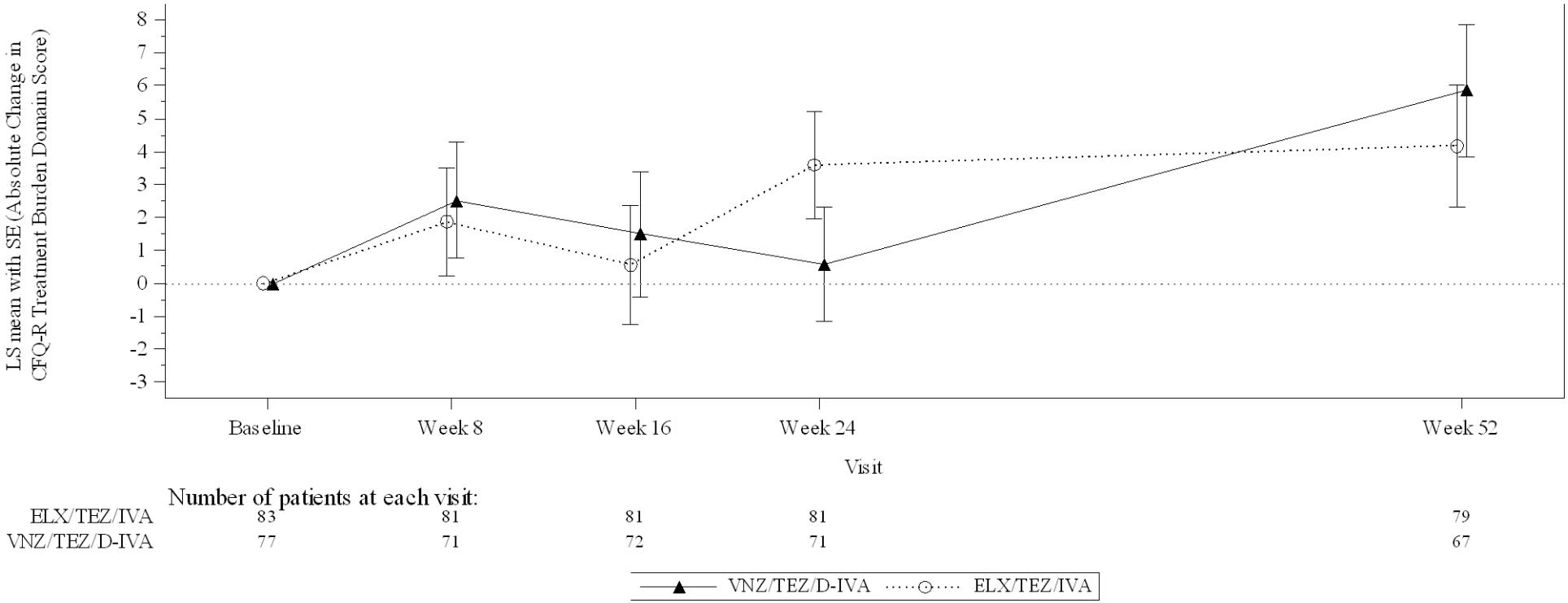
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female



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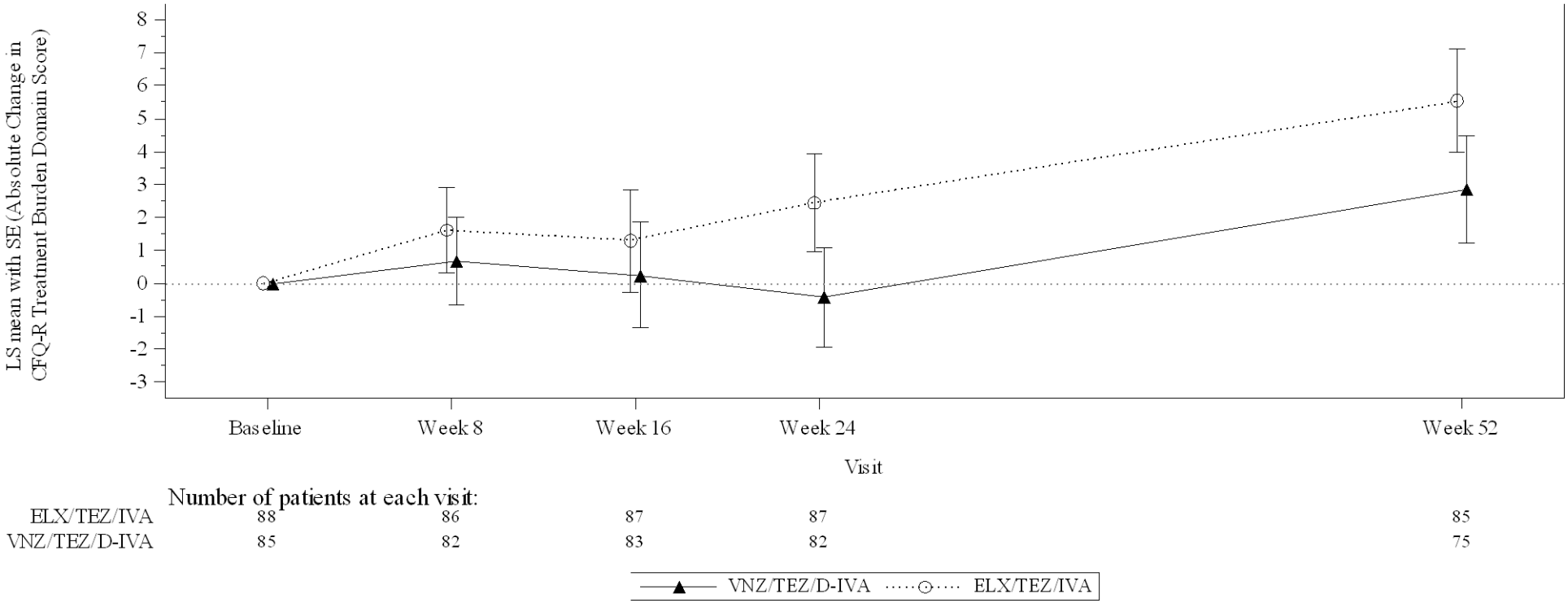
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America



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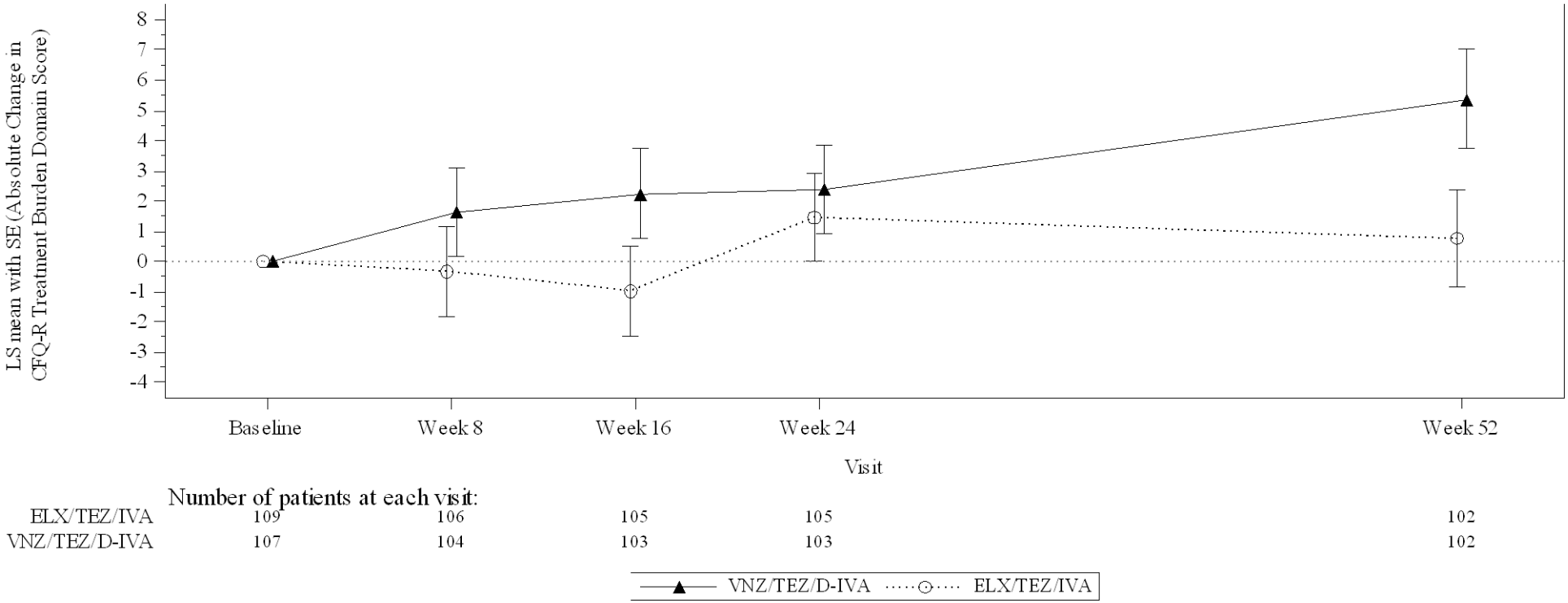
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World



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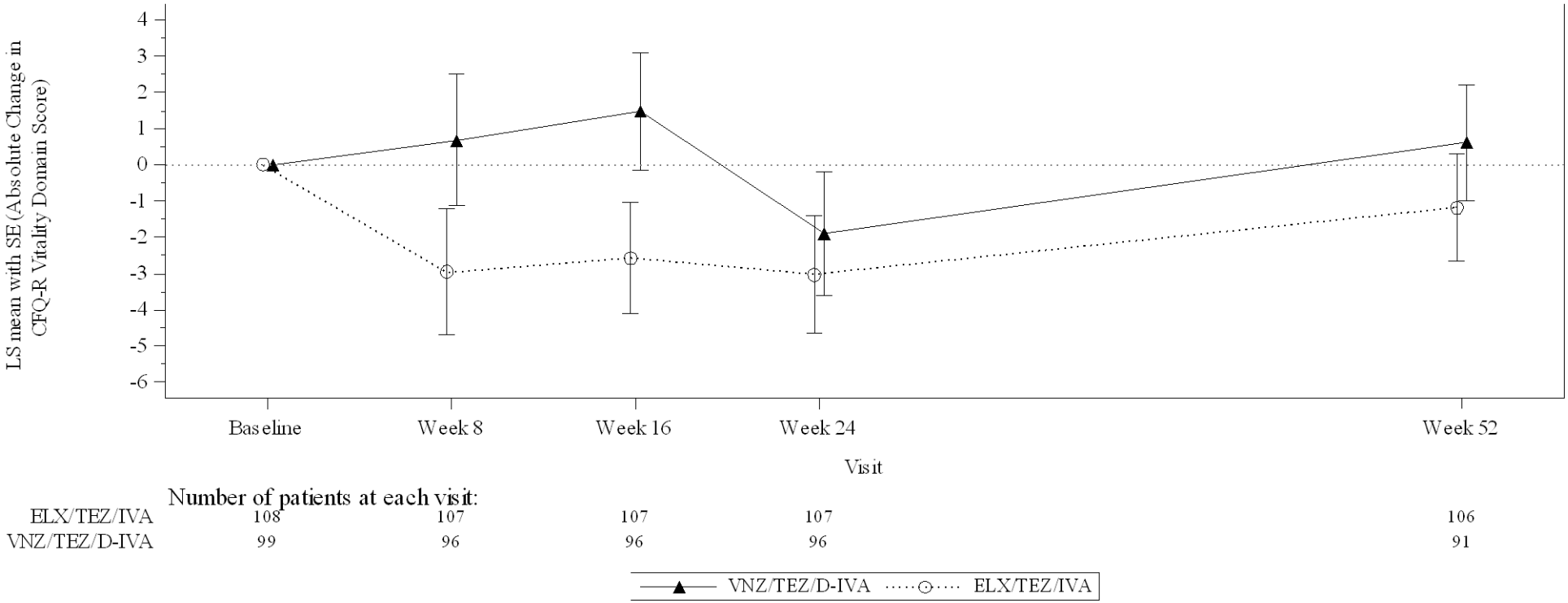
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
ppFEV$_1$ at baseline <70 %



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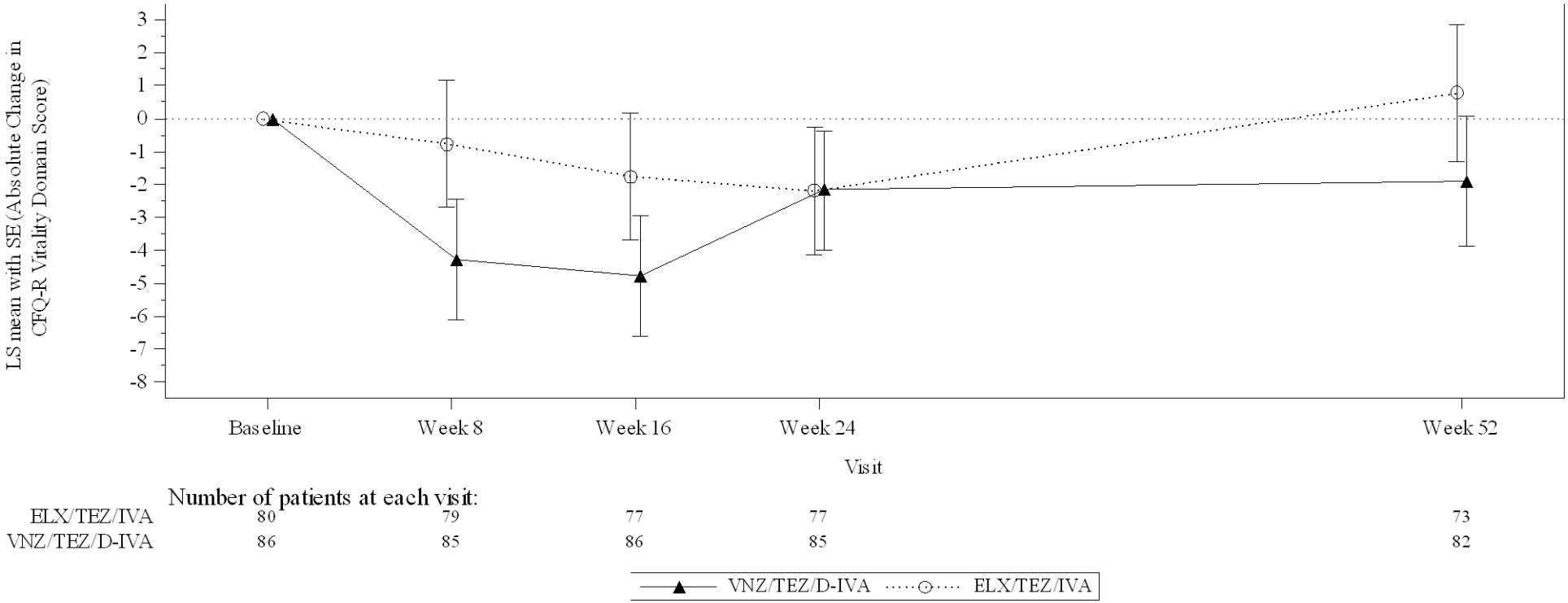
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
ppFEV$_1$ at baseline ≥70 %



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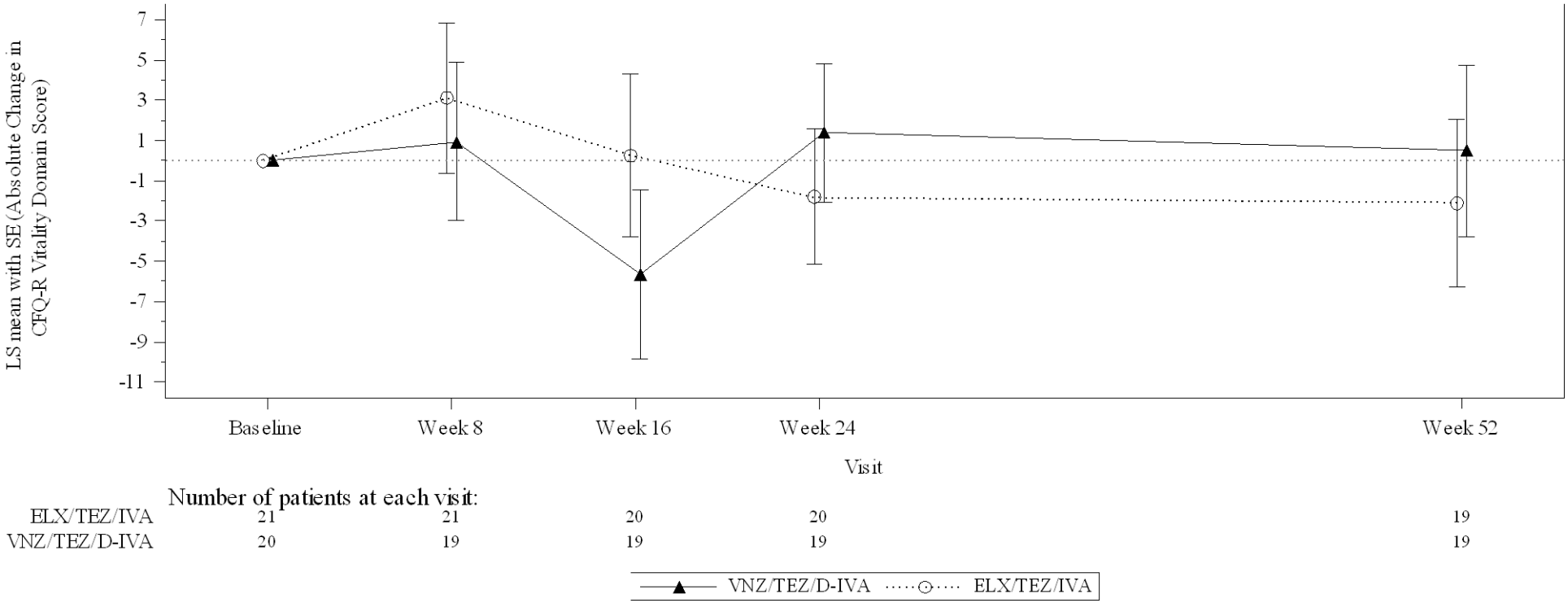
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years



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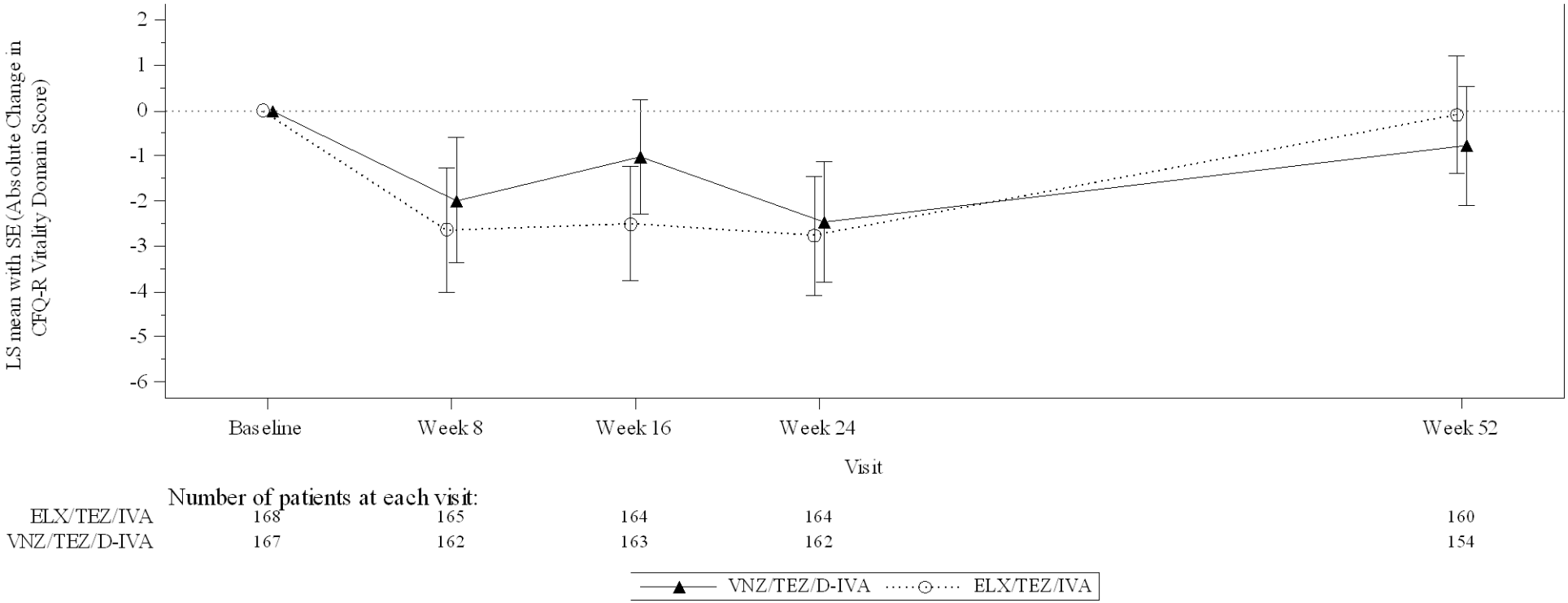
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years



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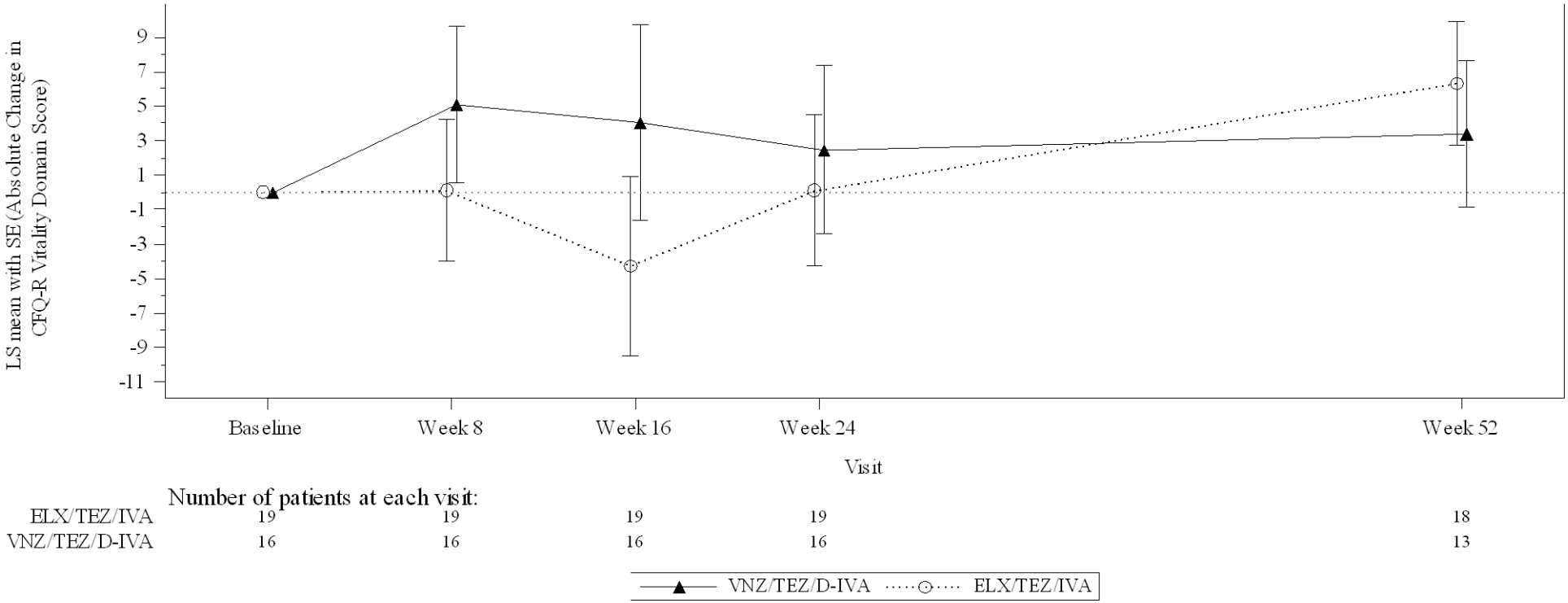
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L



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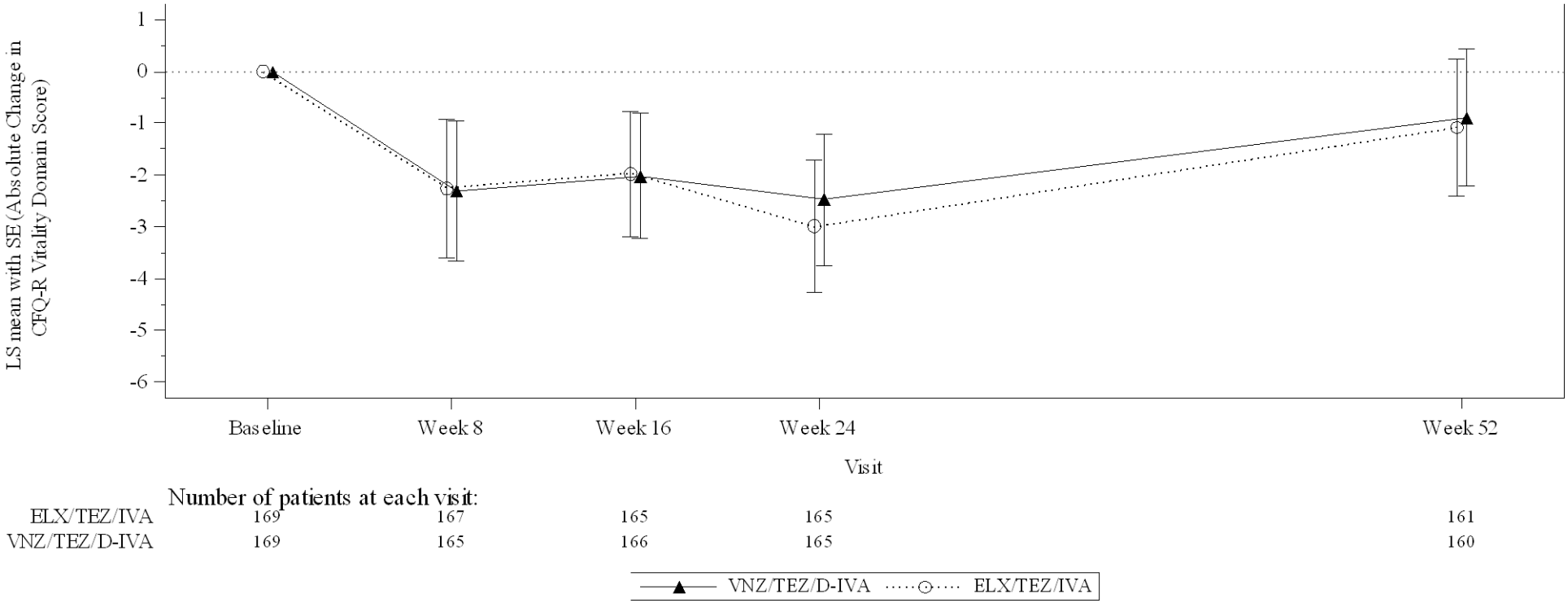
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L



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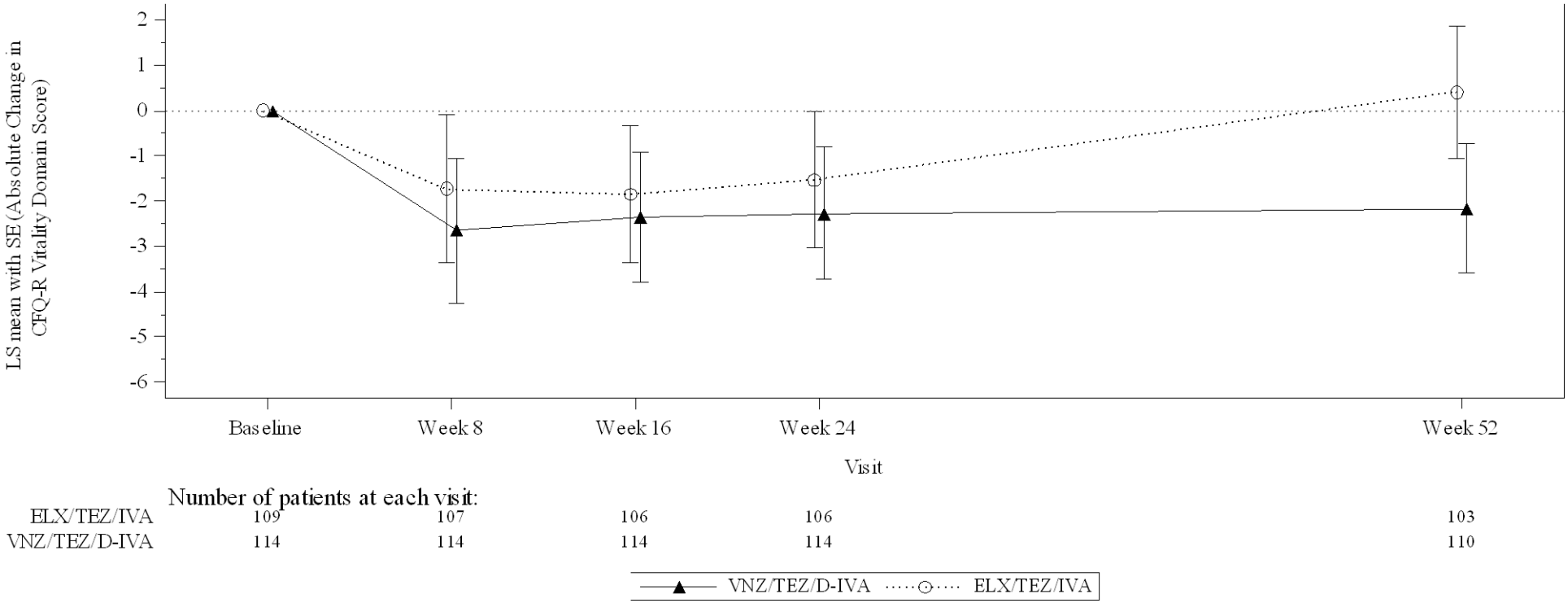
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male



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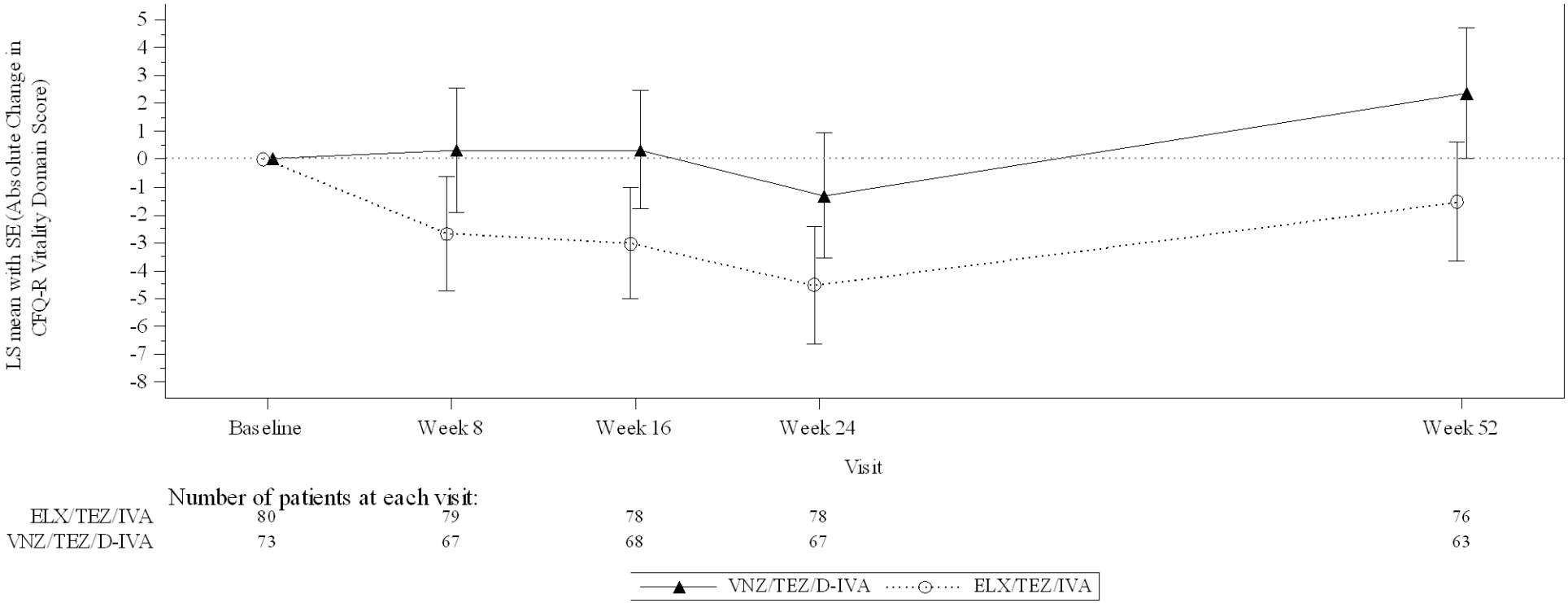
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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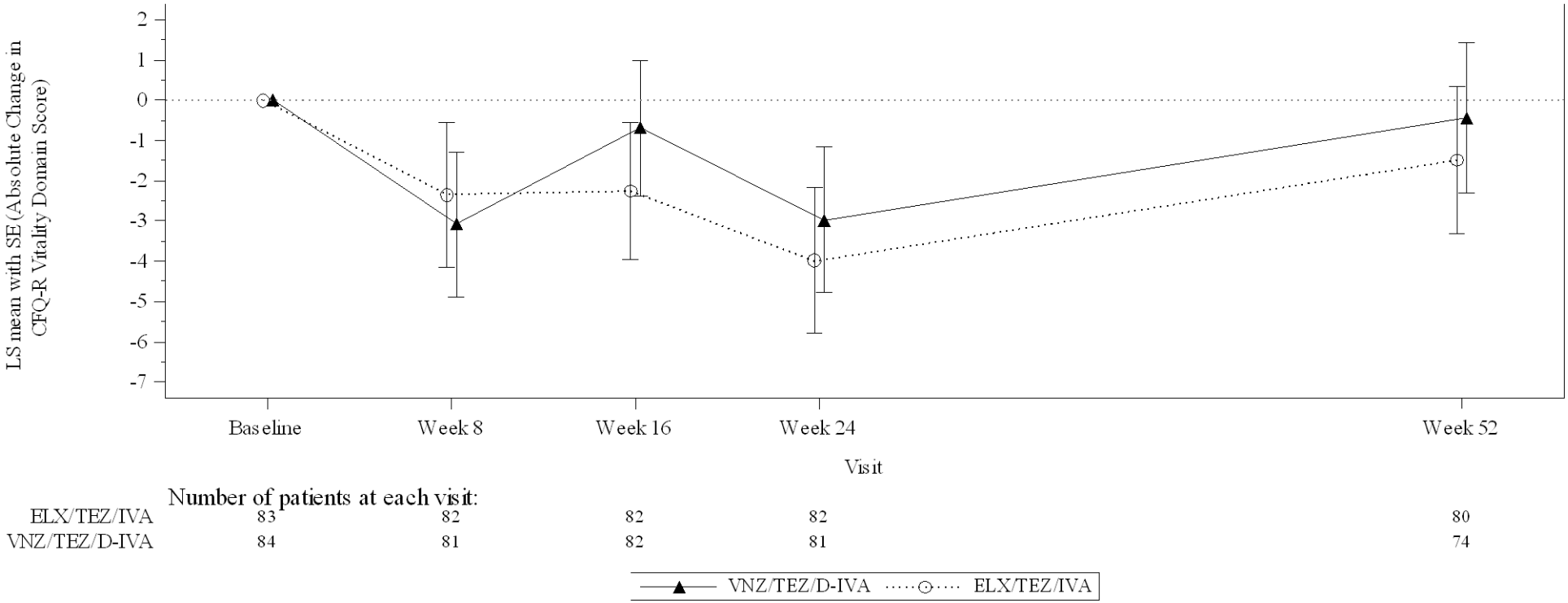
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = North America



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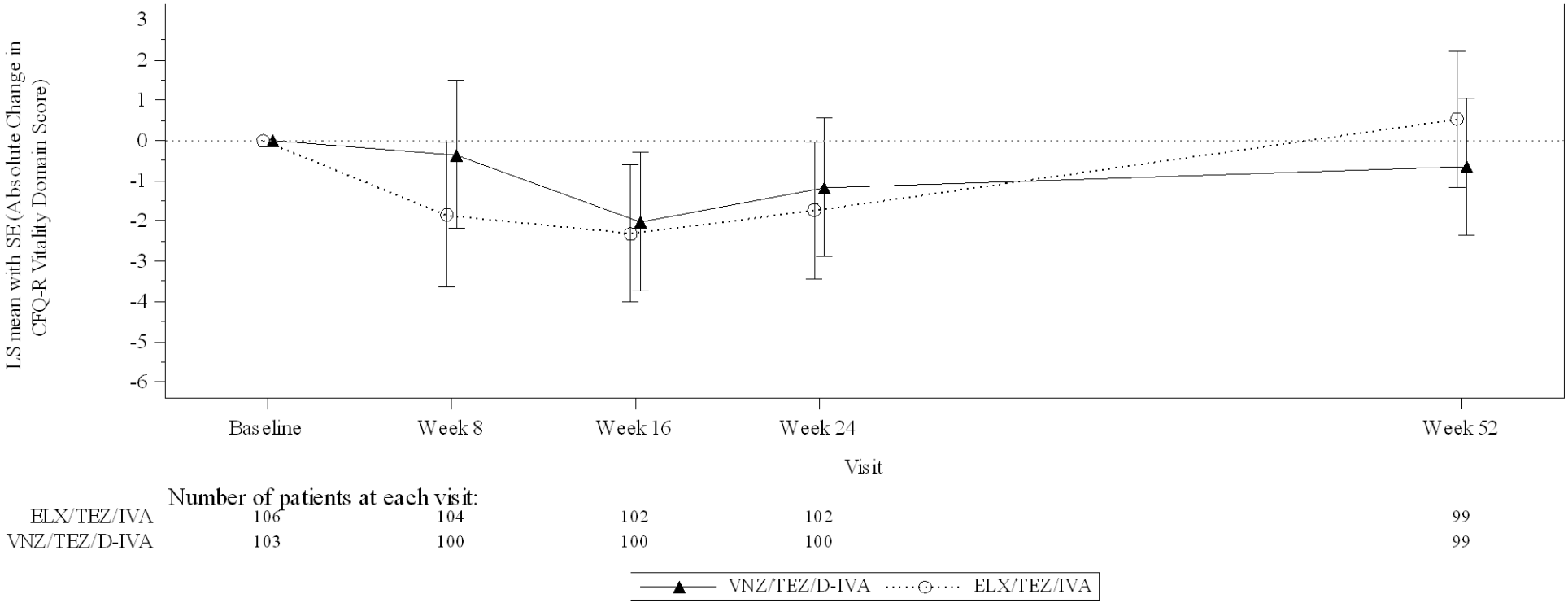
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World



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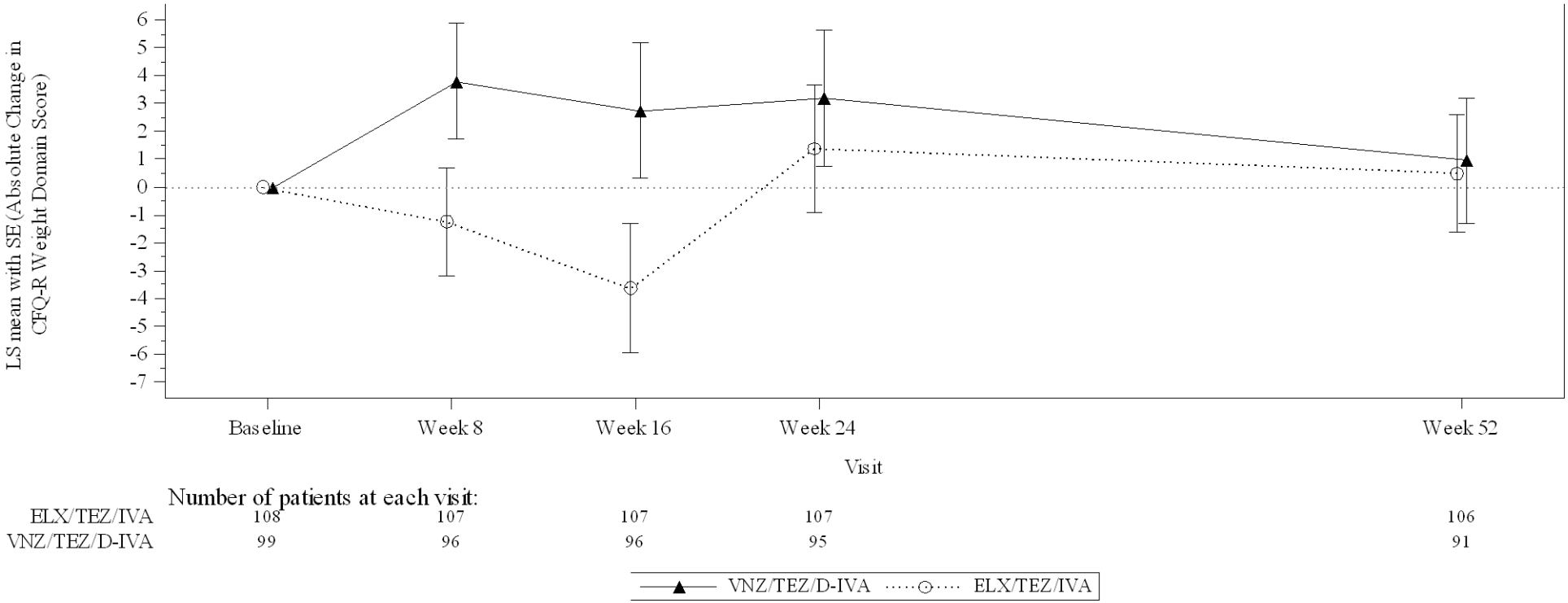
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
ppFEV$_1$ at baseline <70 %



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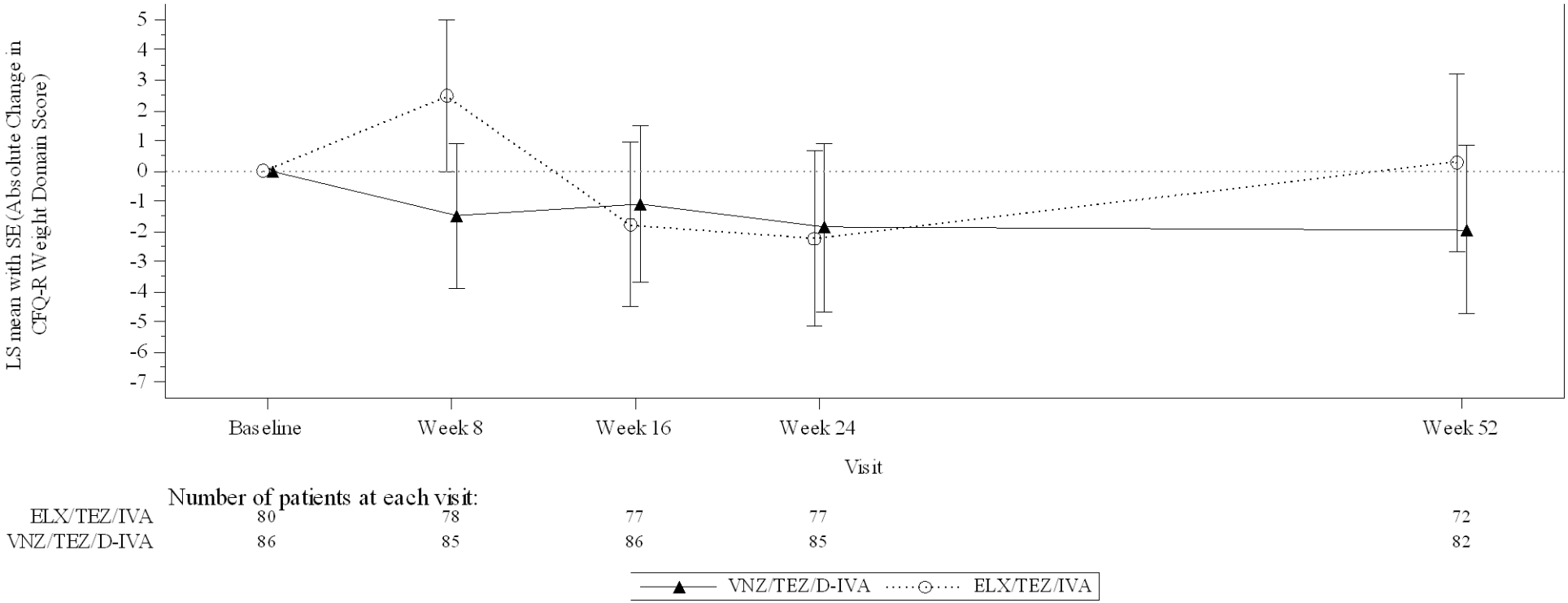
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
ppFEV$_1$ at baseline ≥70 %



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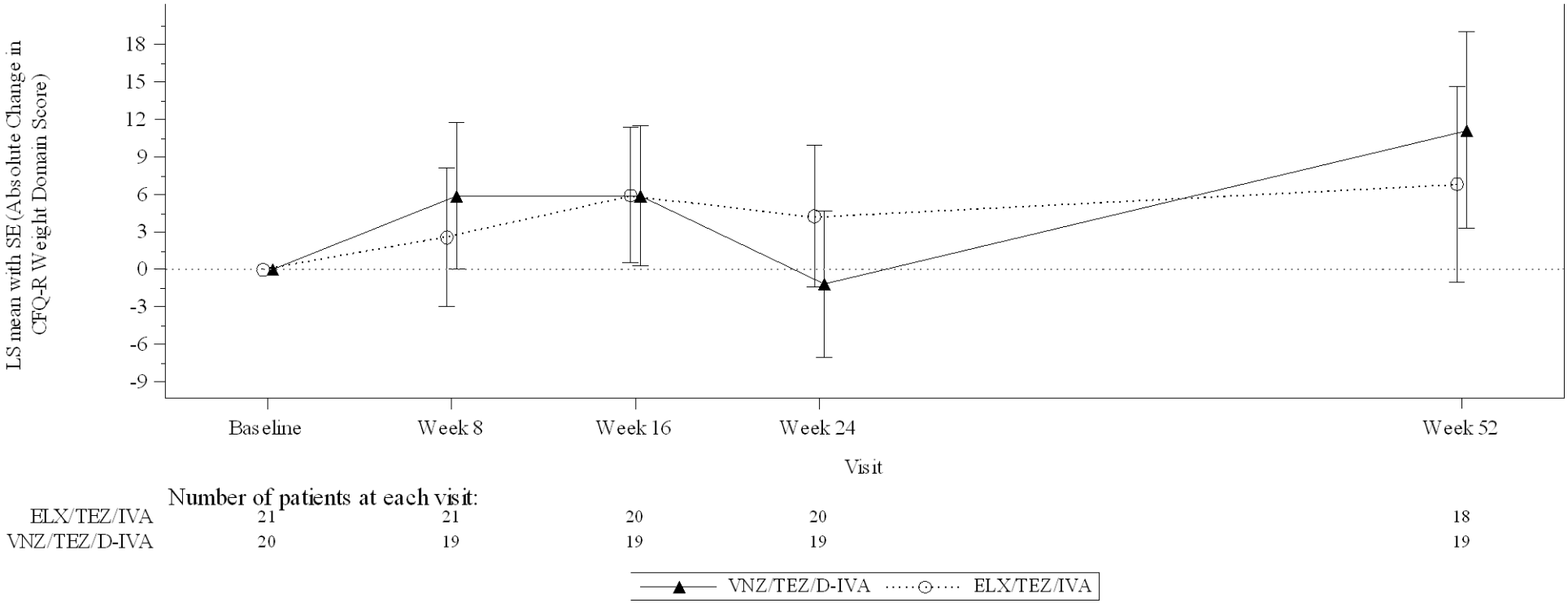
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years



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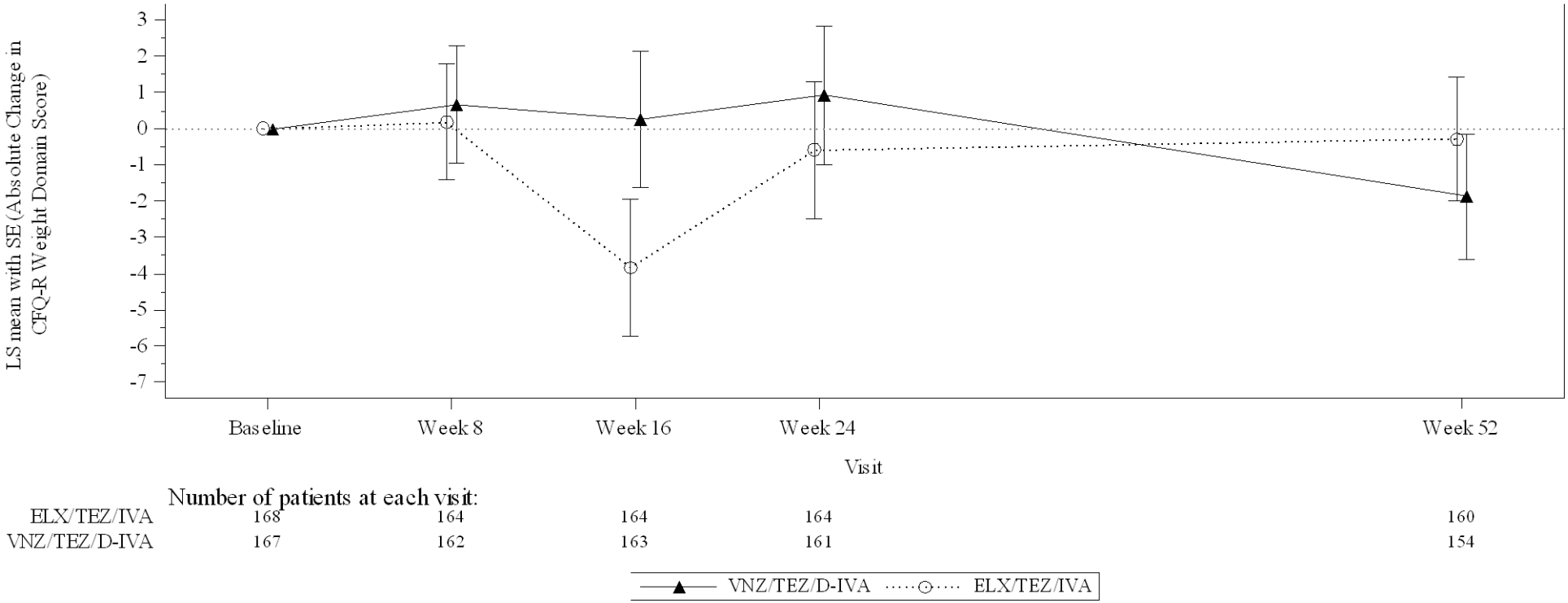
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years



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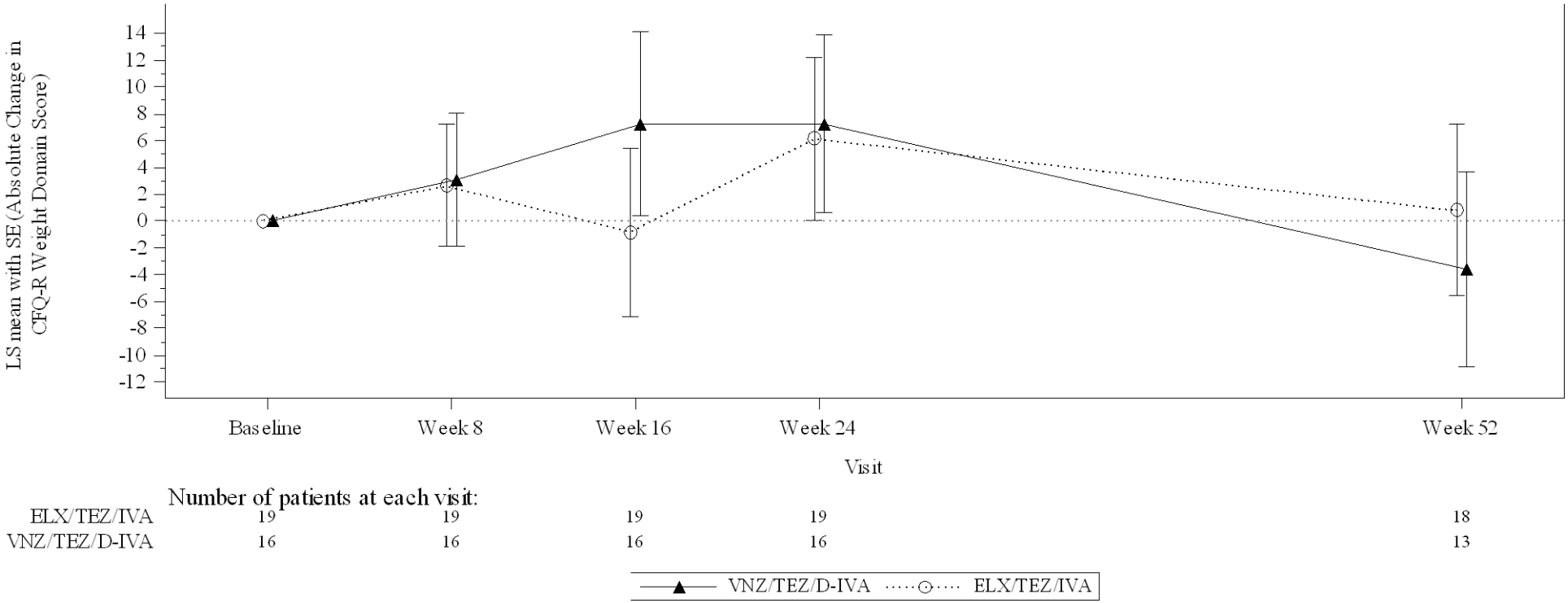
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L



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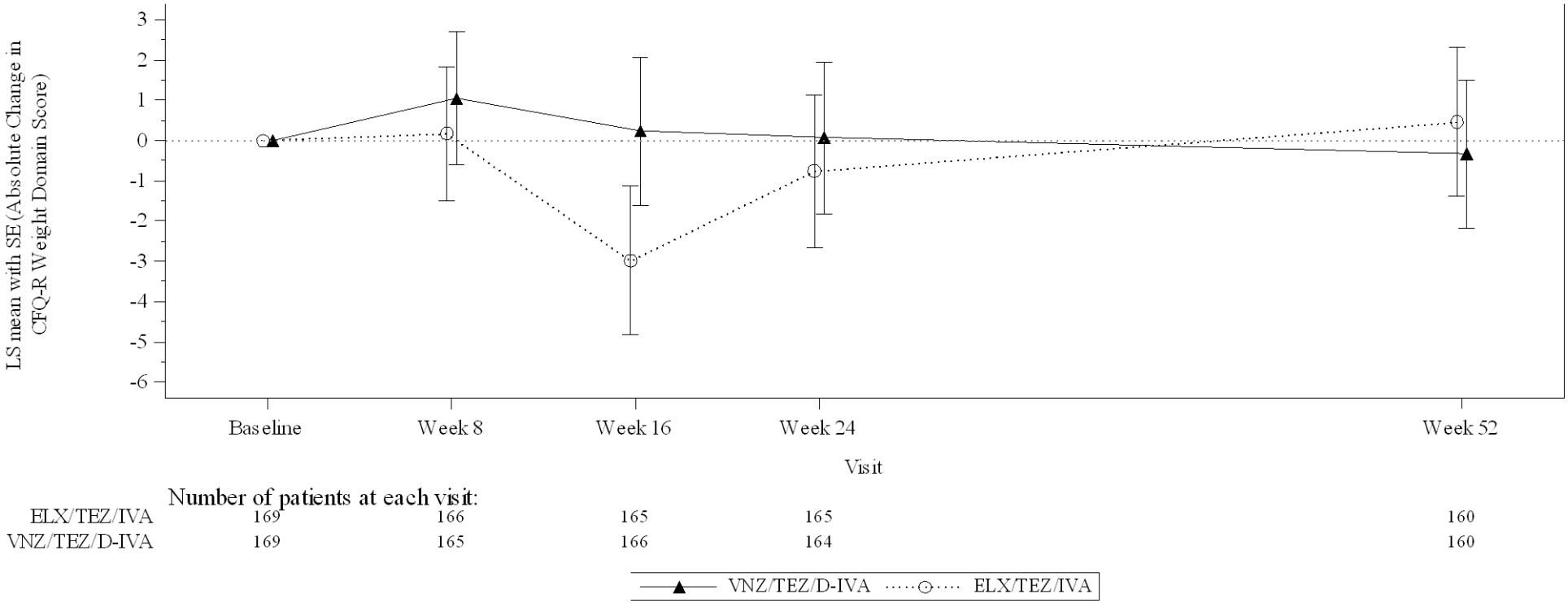
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L



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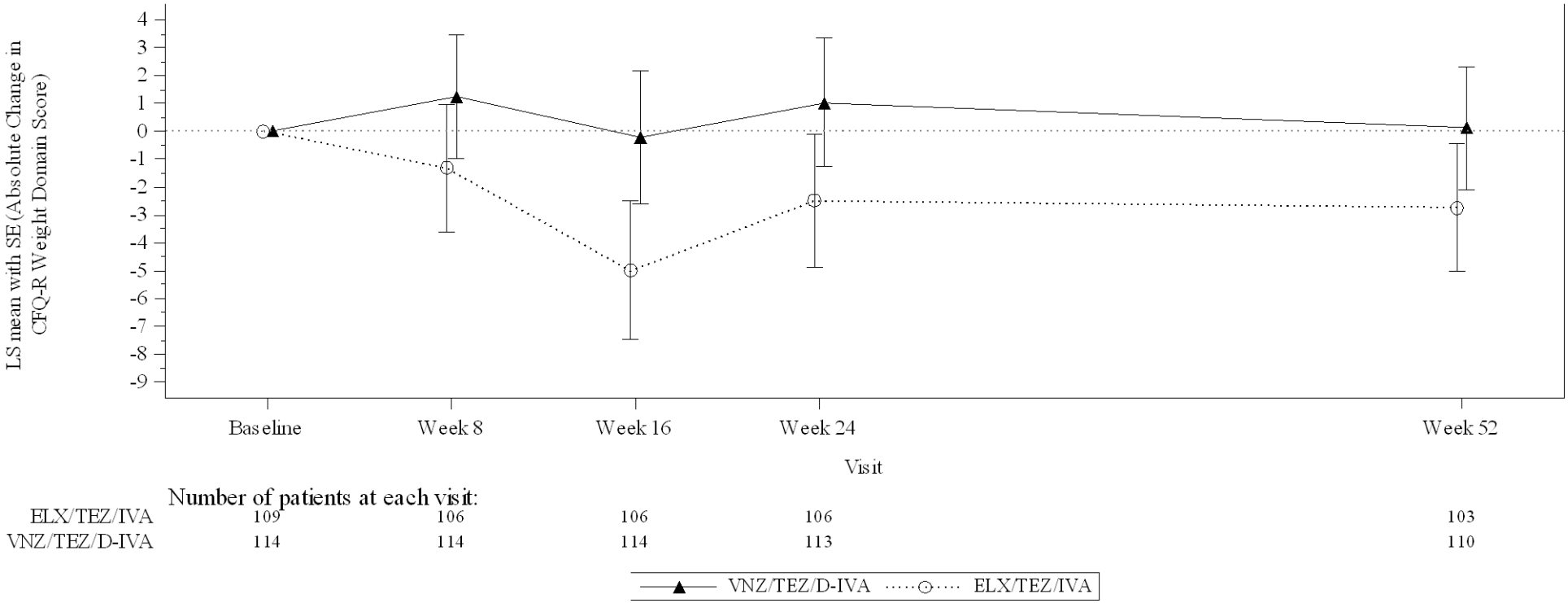
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Male



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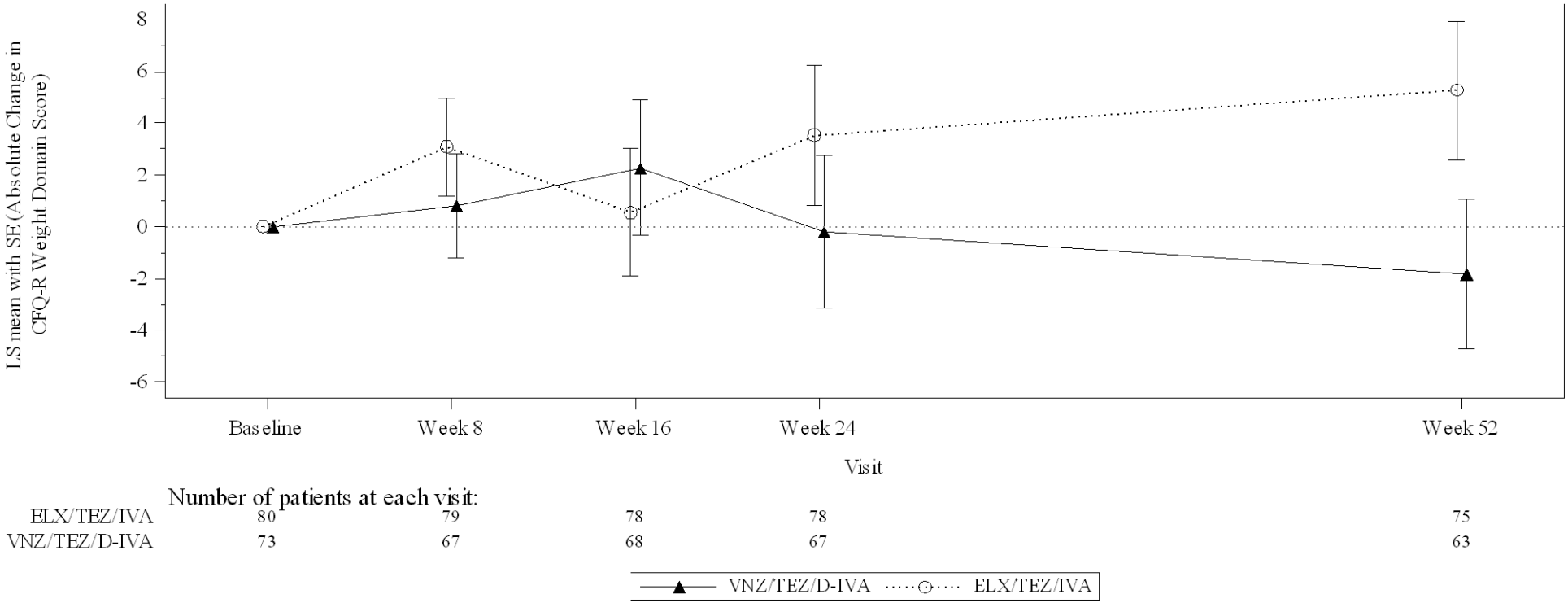
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Female



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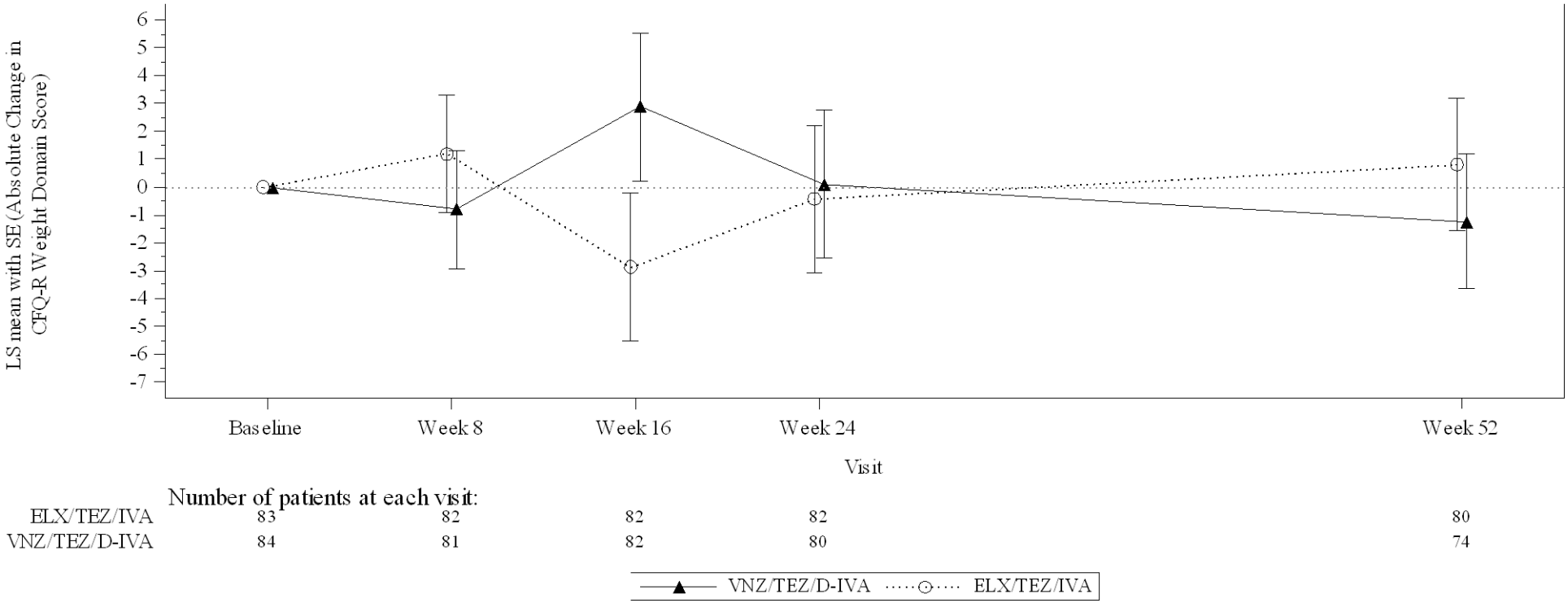
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = North America



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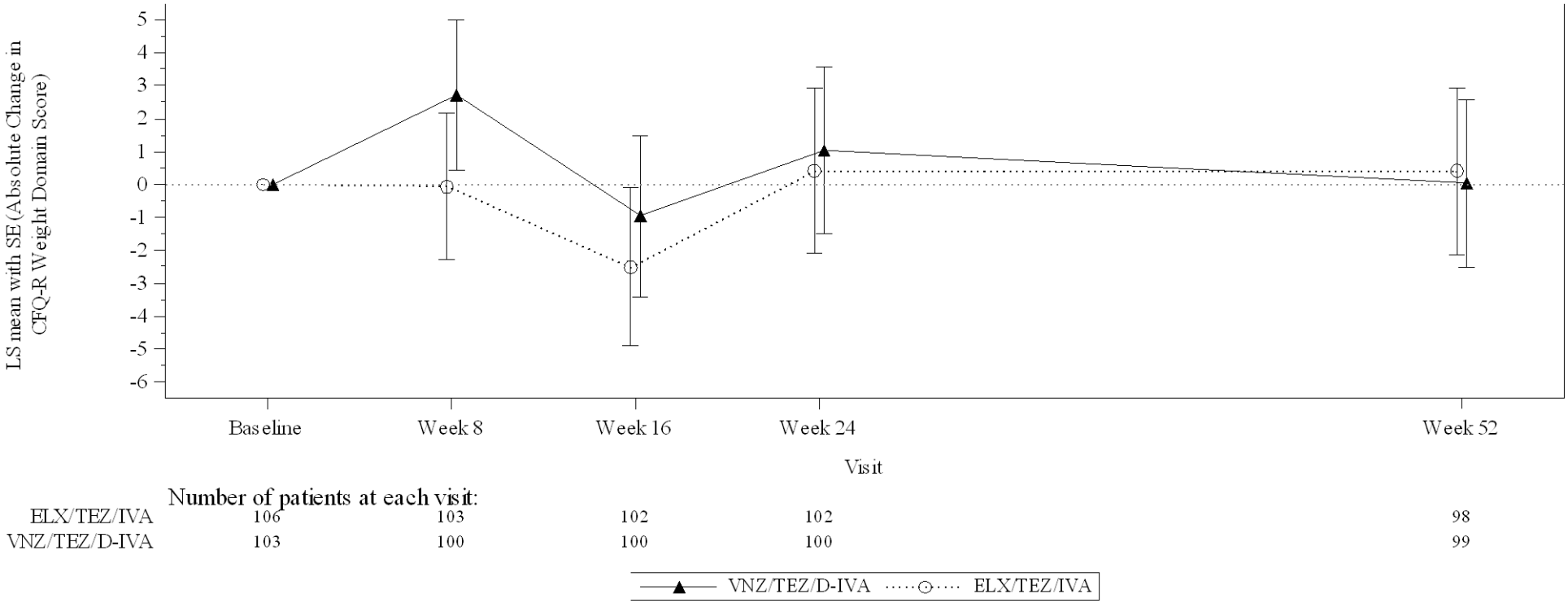
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World



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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-ag12-52wks-sub-102.sas Creation: 17DEC2024 16:46

Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-sub-102.sas Creation: 19DEC2024 20:56

Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration (Parents/Caregivers Form)
ppFEV$_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-sub-102.sas Creation: 19DEC2024 20:56

Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-sub-102.sas Creation: 19DEC2024 20:56

Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-sub-102.sas Creation: 19DEC2024 20:56

Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-sub-102.sas Creation: 19DEC2024 20:56

Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-sub-102.sas Creation: 19DEC2024 20:56

Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-sub-102.sas Creation: 19DEC2024 20:56

Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-sub-102.sas Creation: 19DEC2024 20:56

Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-sub-102.sas Creation: 19DEC2024 20:56

Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-sub-102.sas Creation: 19DEC2024 20:56

Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-sub-102.sas Creation: 19DEC2024 20:56

Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: School (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: School (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: School (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: School (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: School (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: School (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: School (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: School (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden (Parents/Caregivers Form)
ppFEV$_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.

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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-sub-102.sas Creation: 19DEC2024 20:56

Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-sub-102.sas Creation: 19DEC2024 20:56

Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-sub-102.sas Creation: 19DEC2024 20:56

Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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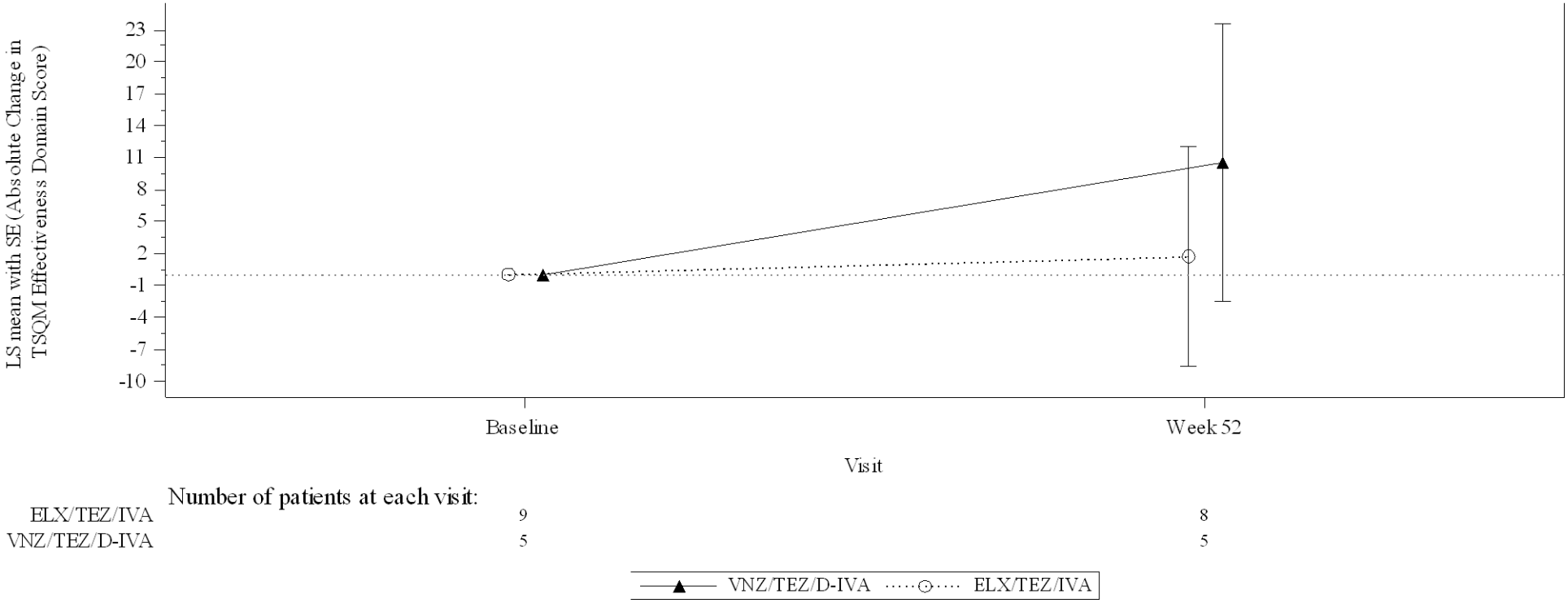
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfqr-cg-52wks-sub-102.sas Creation: 19DEC2024 20:56

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
ppFEV$_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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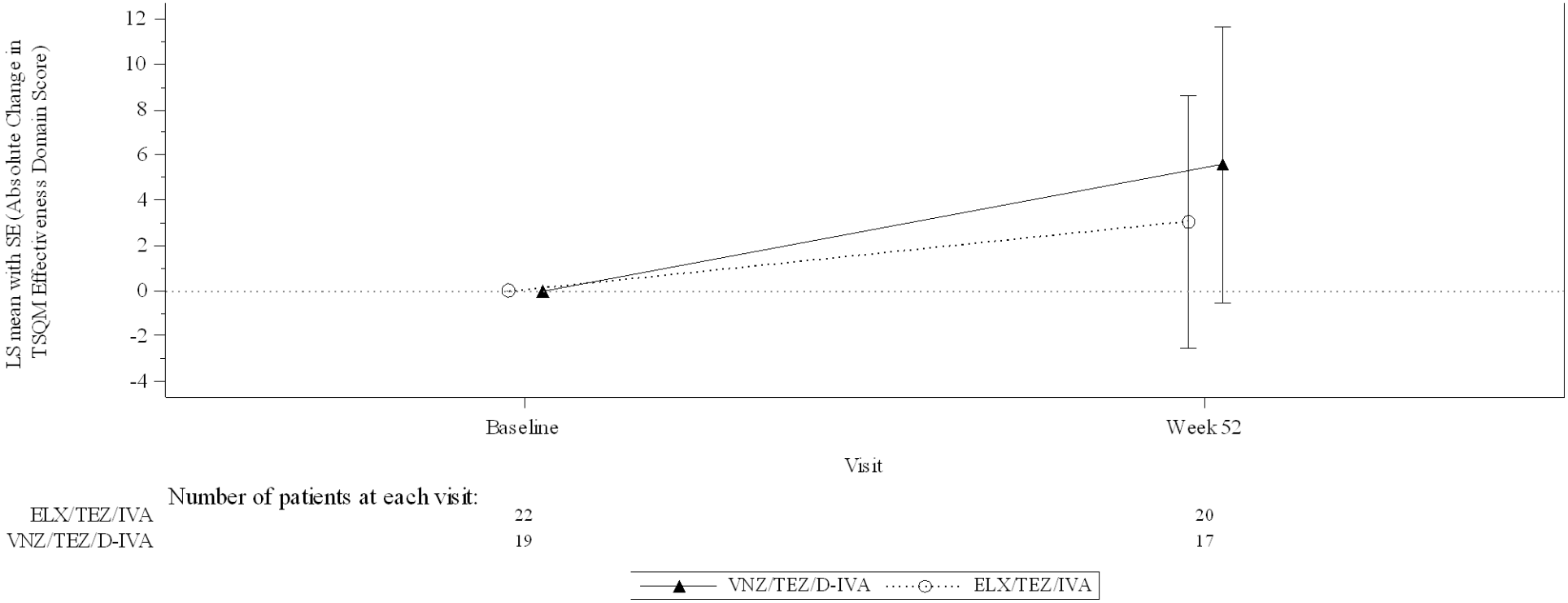
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
ppFEV$_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Age at screening <18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Age at screening ≥18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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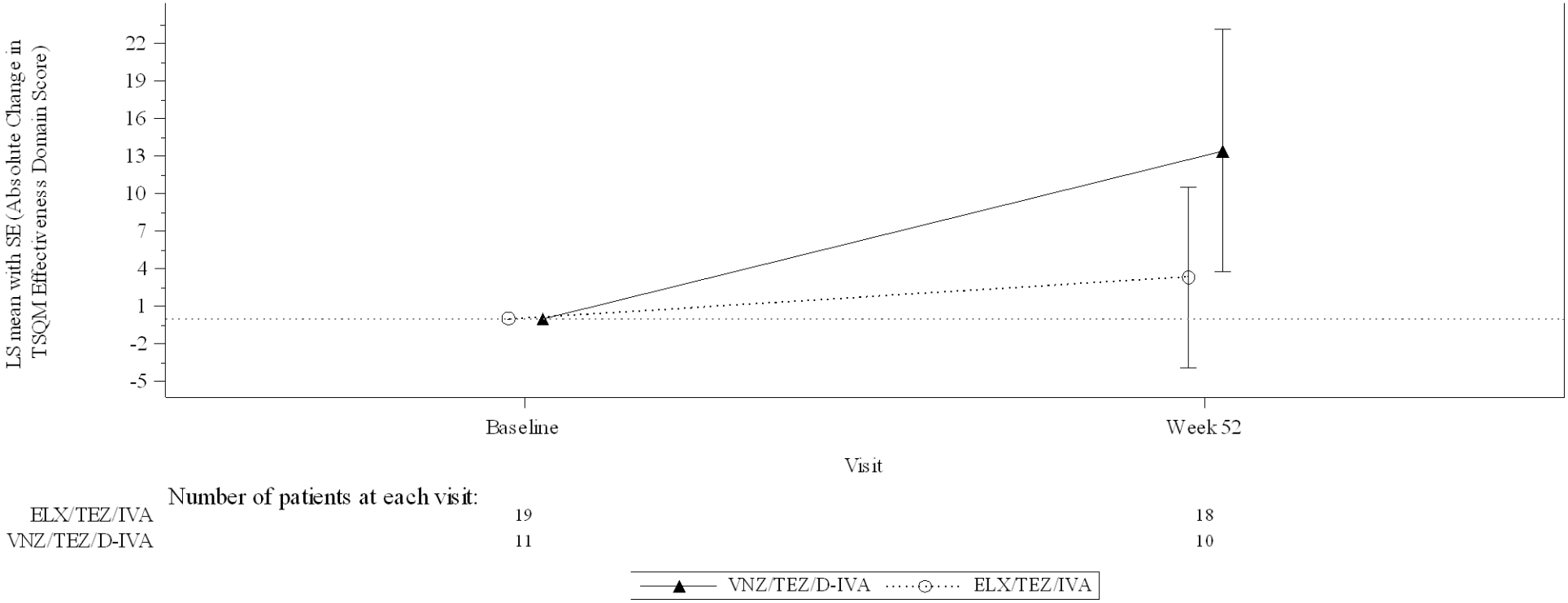
Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Female

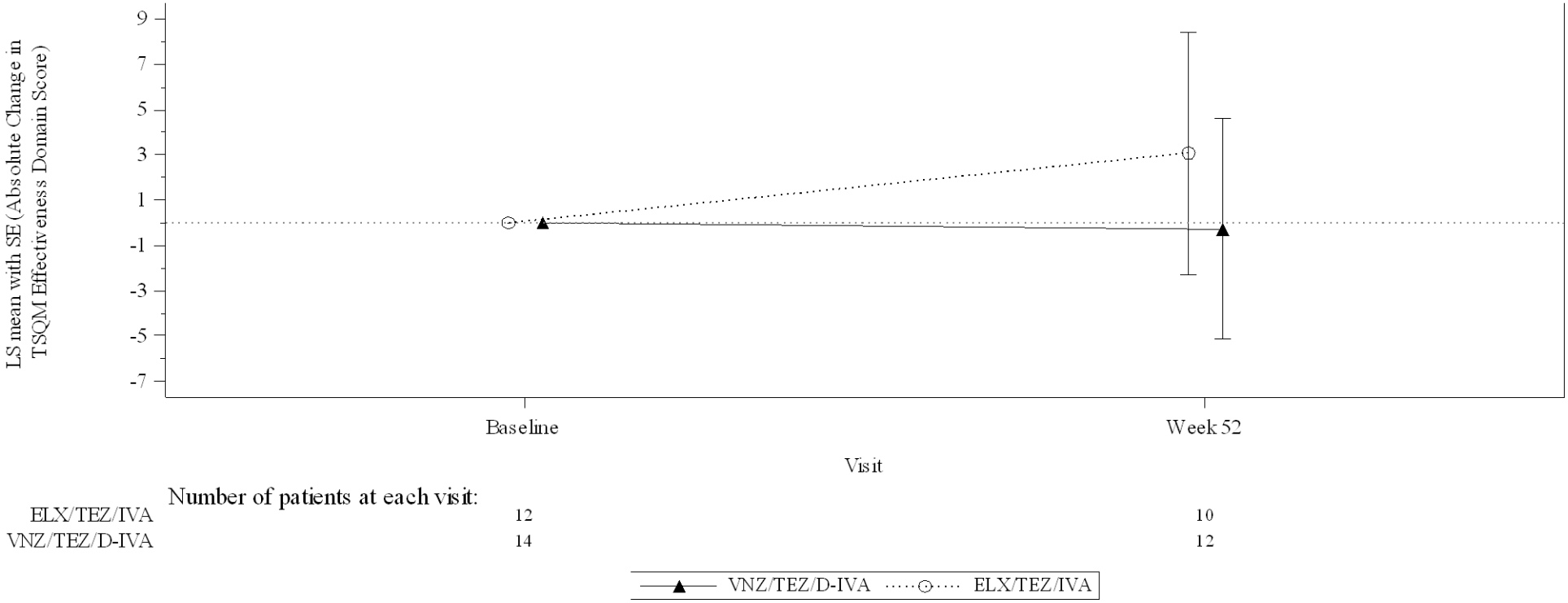

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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = North America

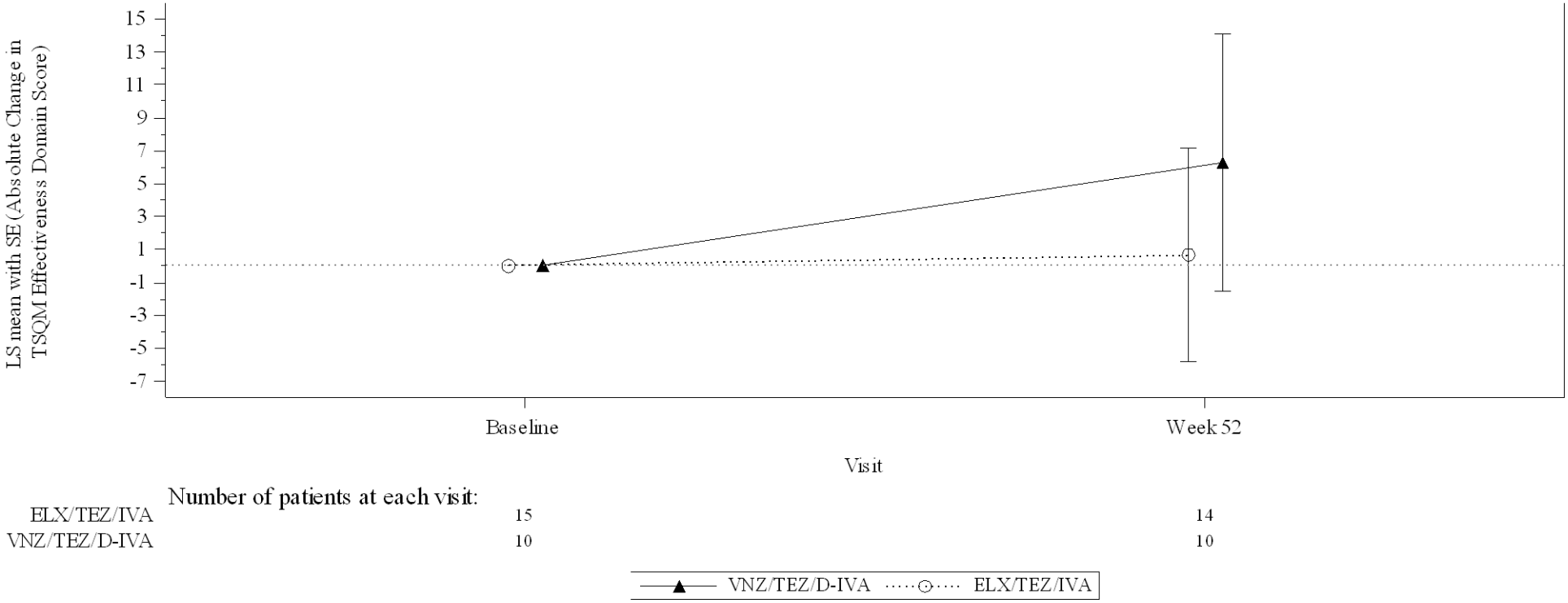

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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = Rest of World

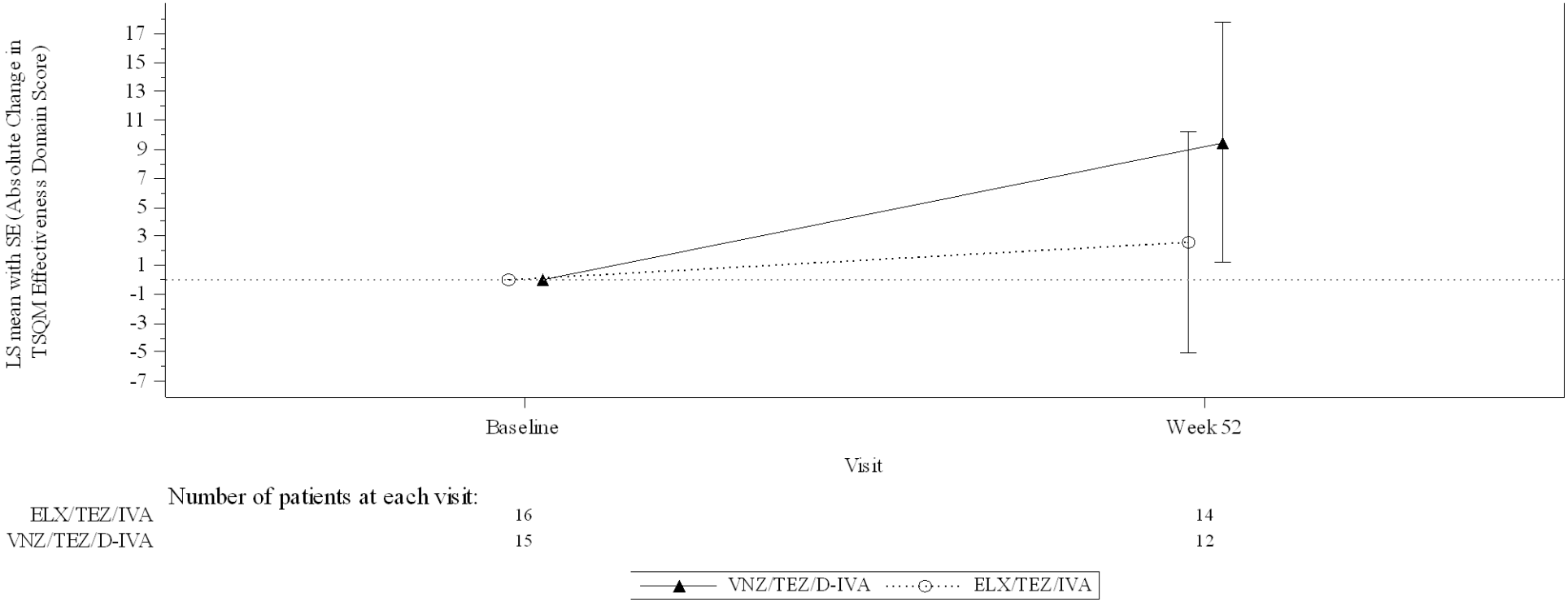

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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
ppFEV$_1$ at baseline <70 %

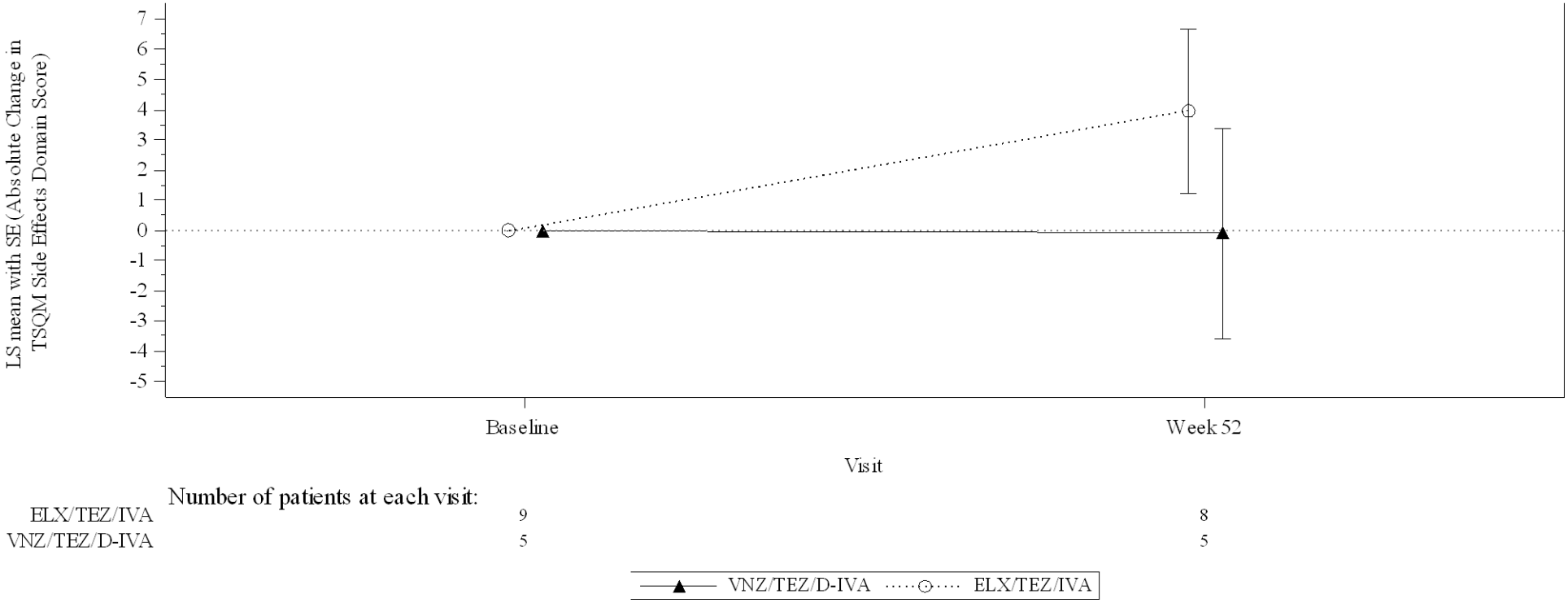

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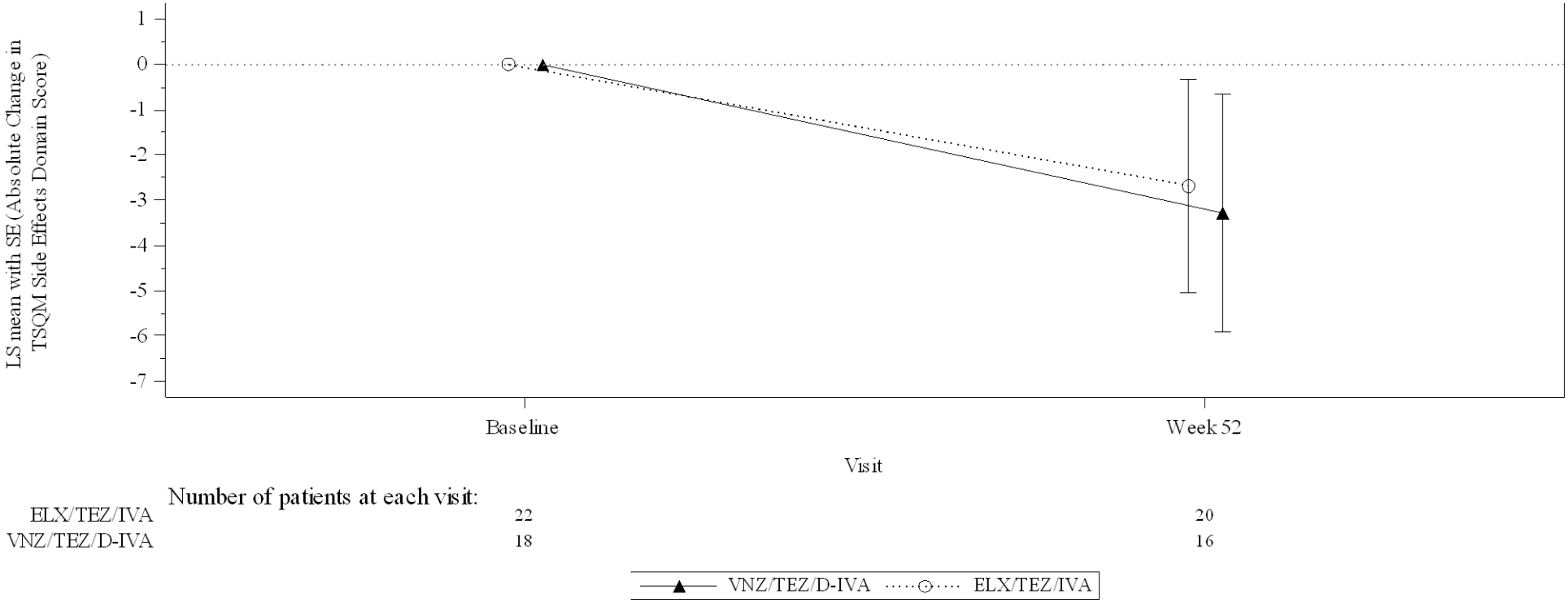
Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
ppFEV$_1$ at baseline ≥70 %



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- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Age at screening <18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Age at screening ≥18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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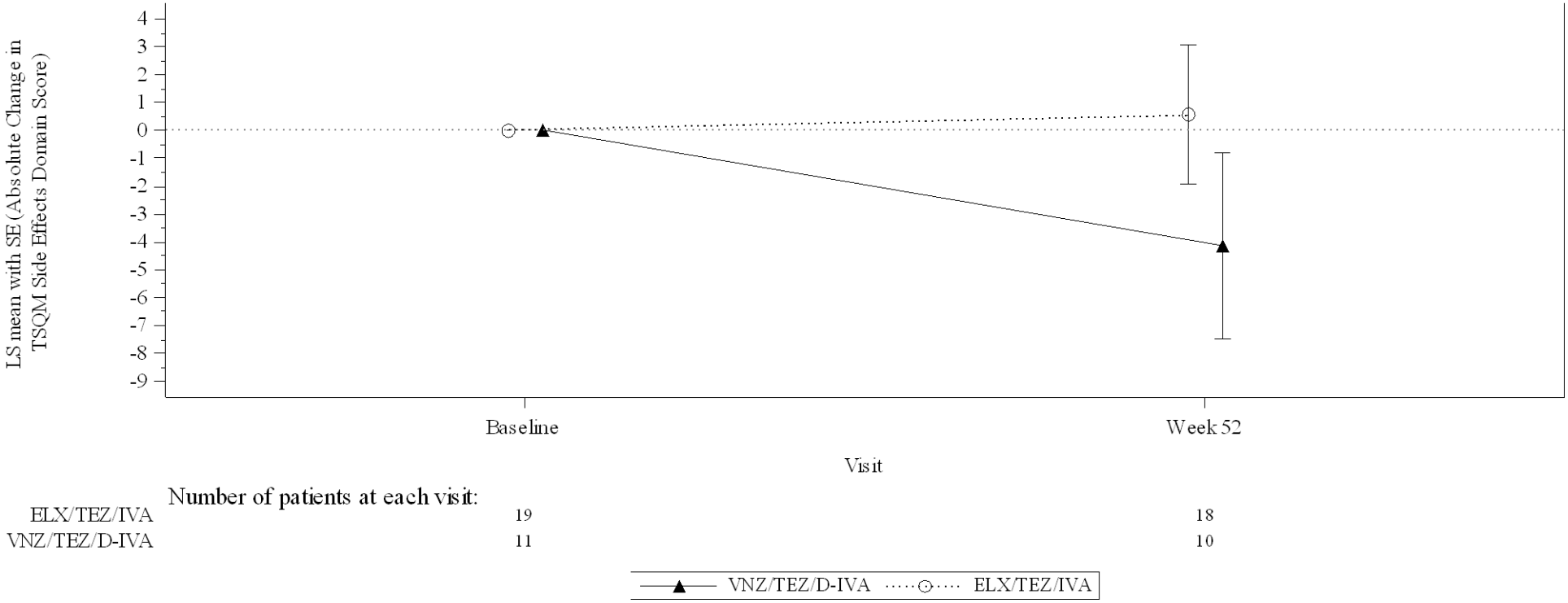
Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Male

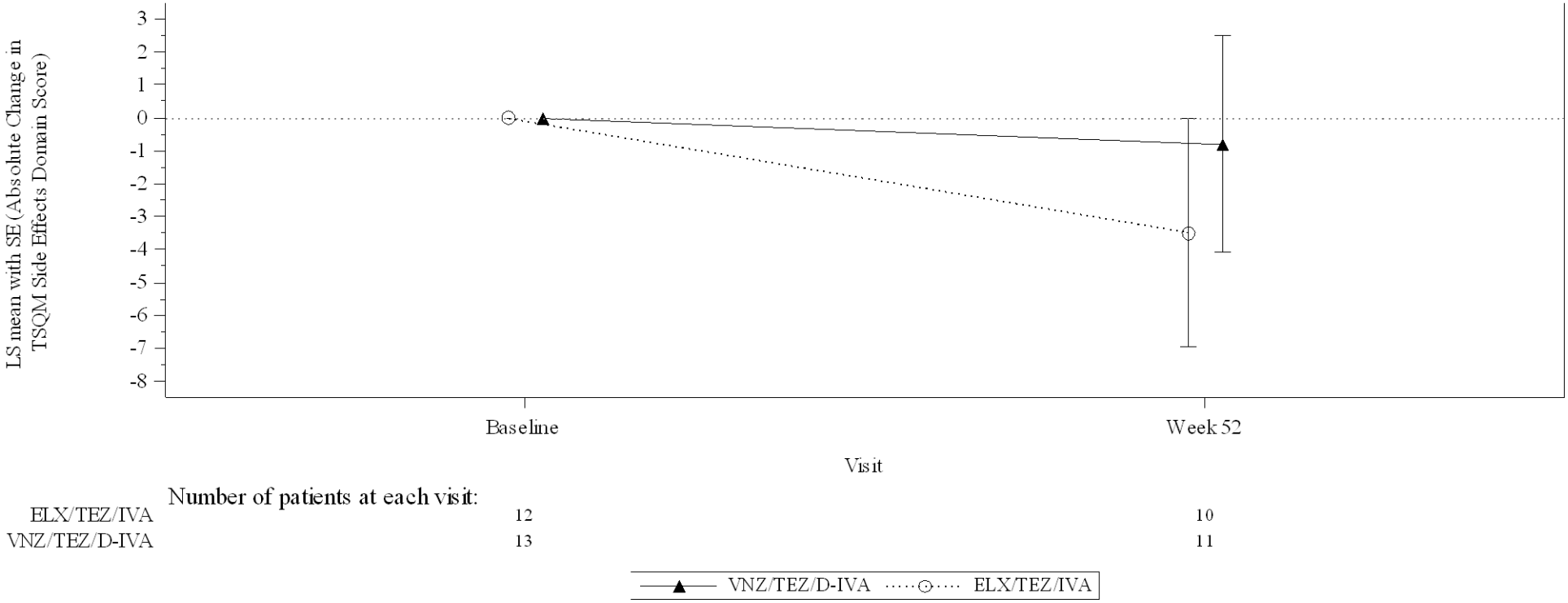


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Female

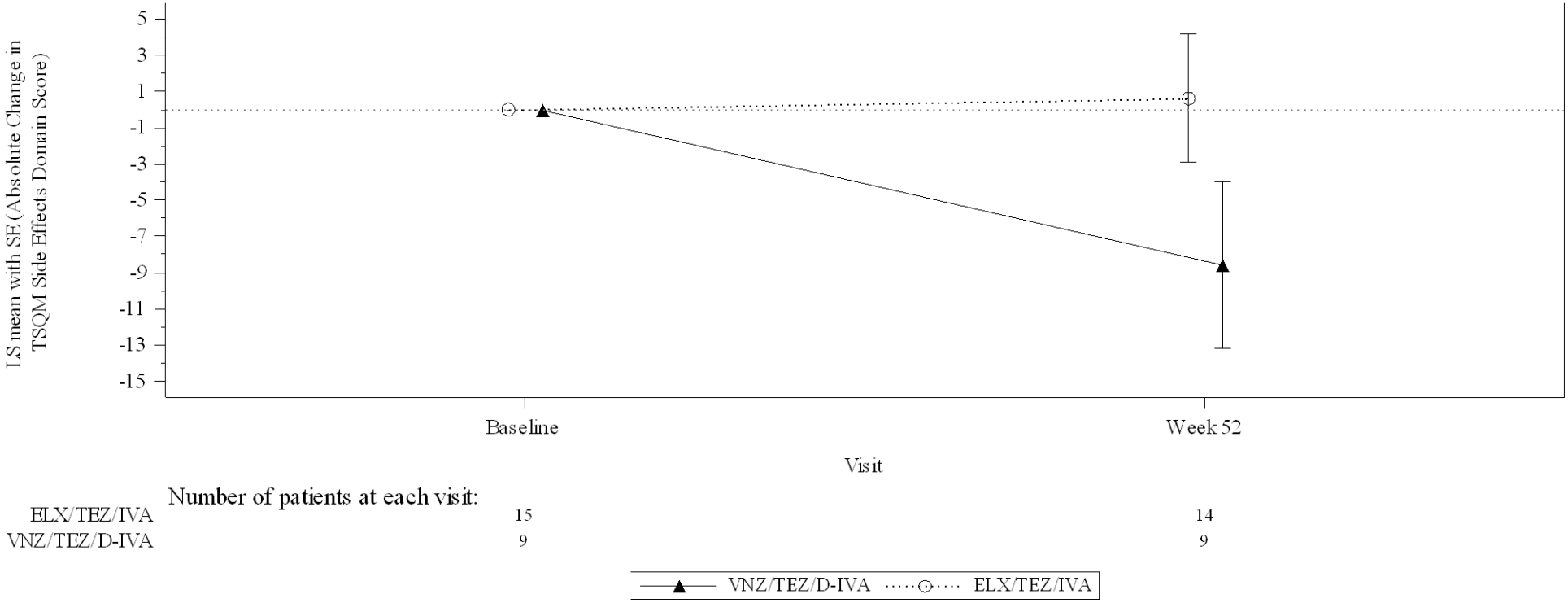


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

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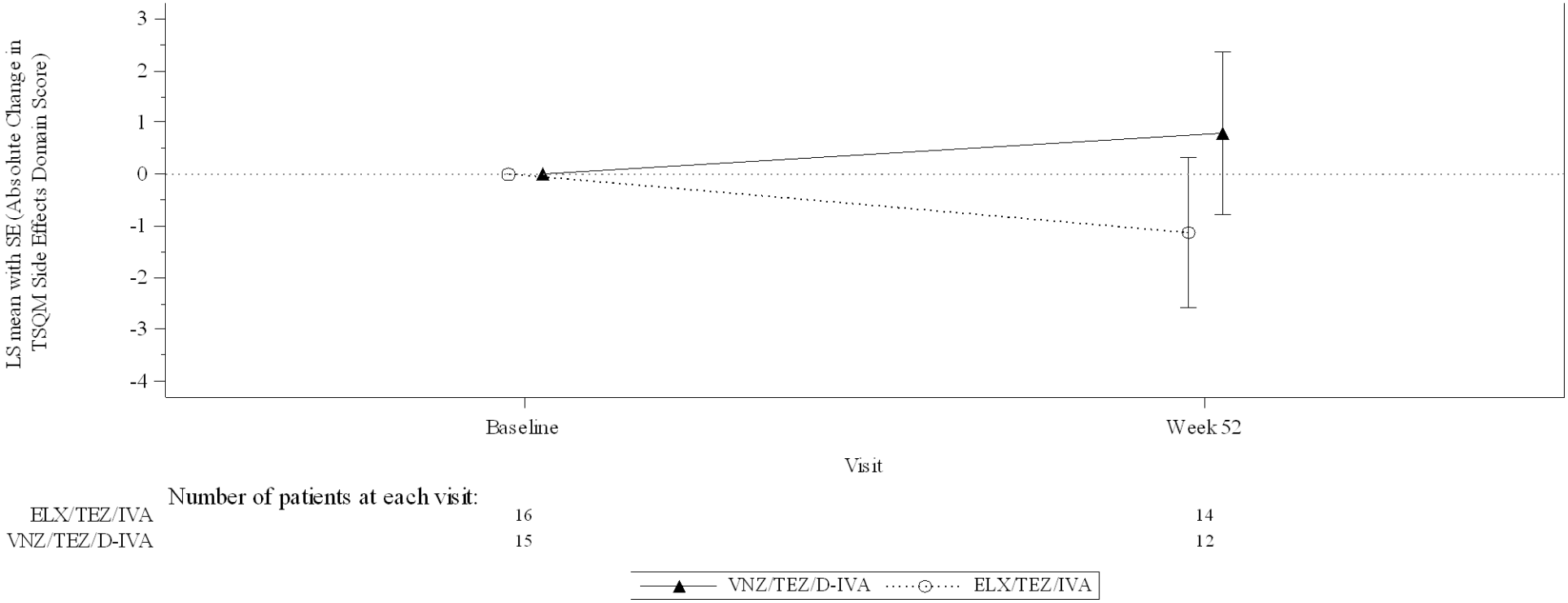
Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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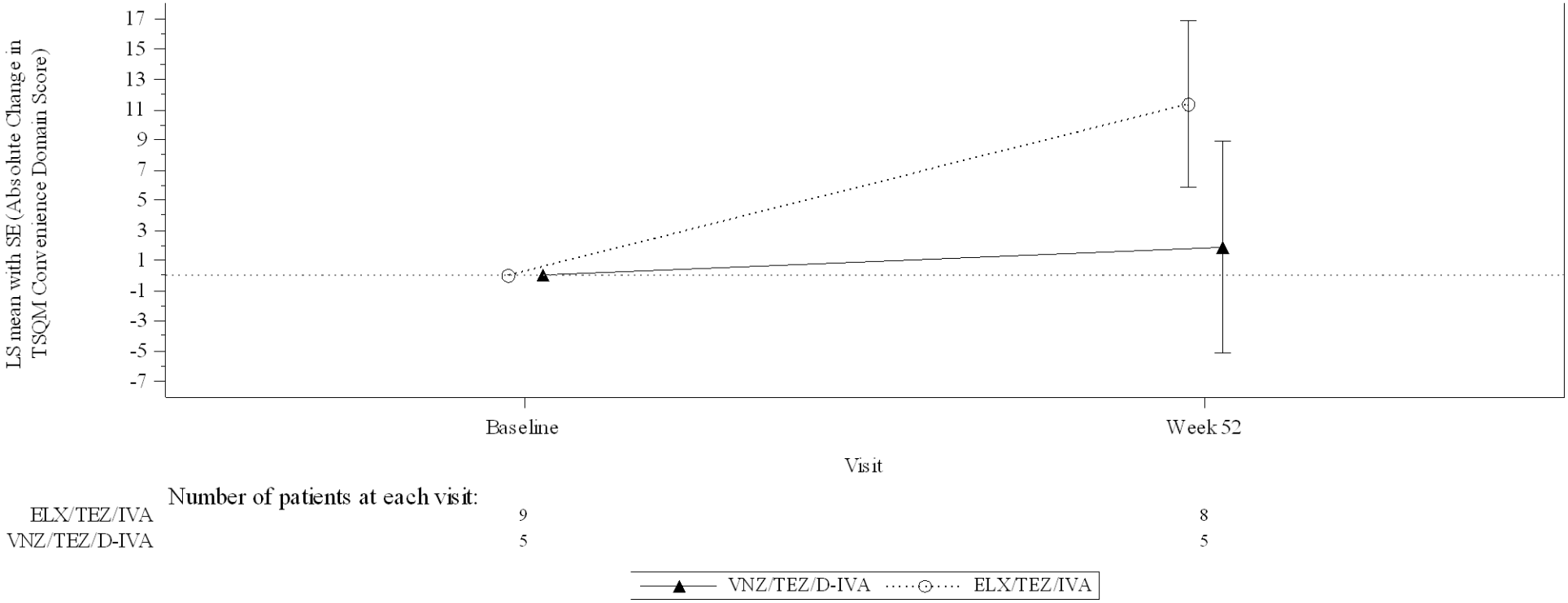
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
ppFEV$_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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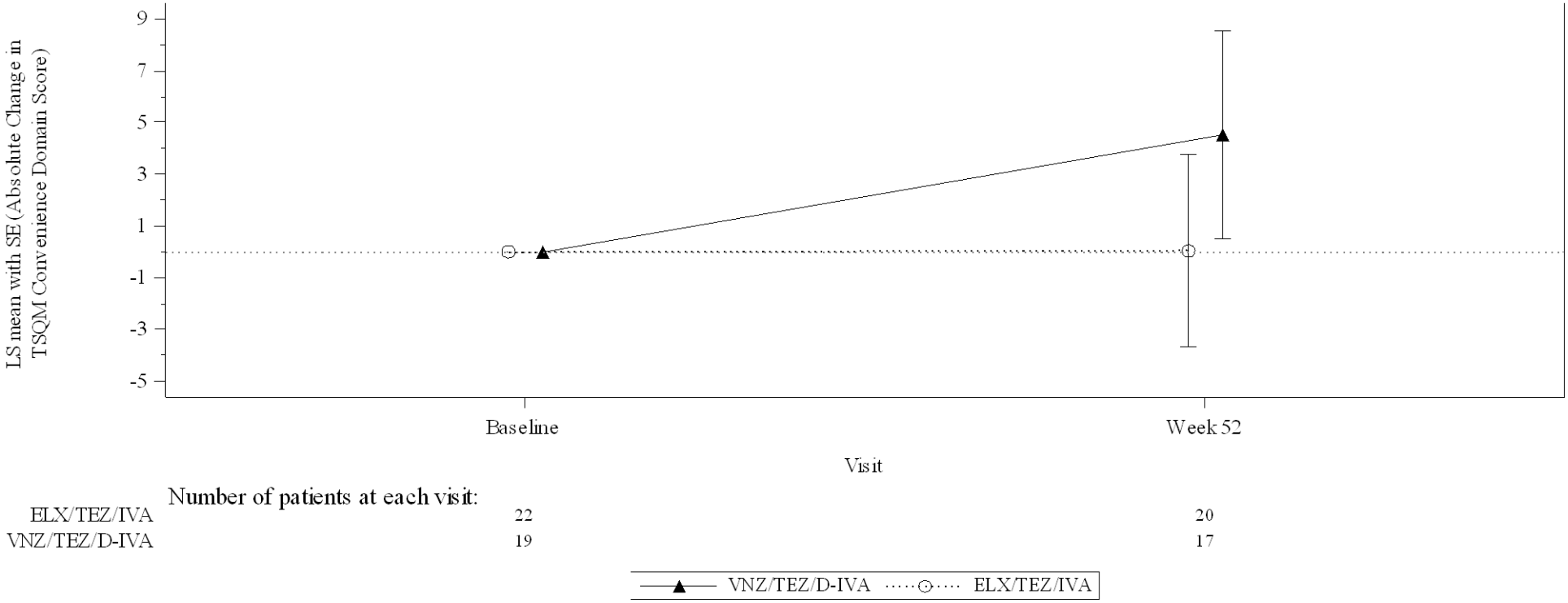
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
ppFEV$_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Age at screening <18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Age at screening ≥18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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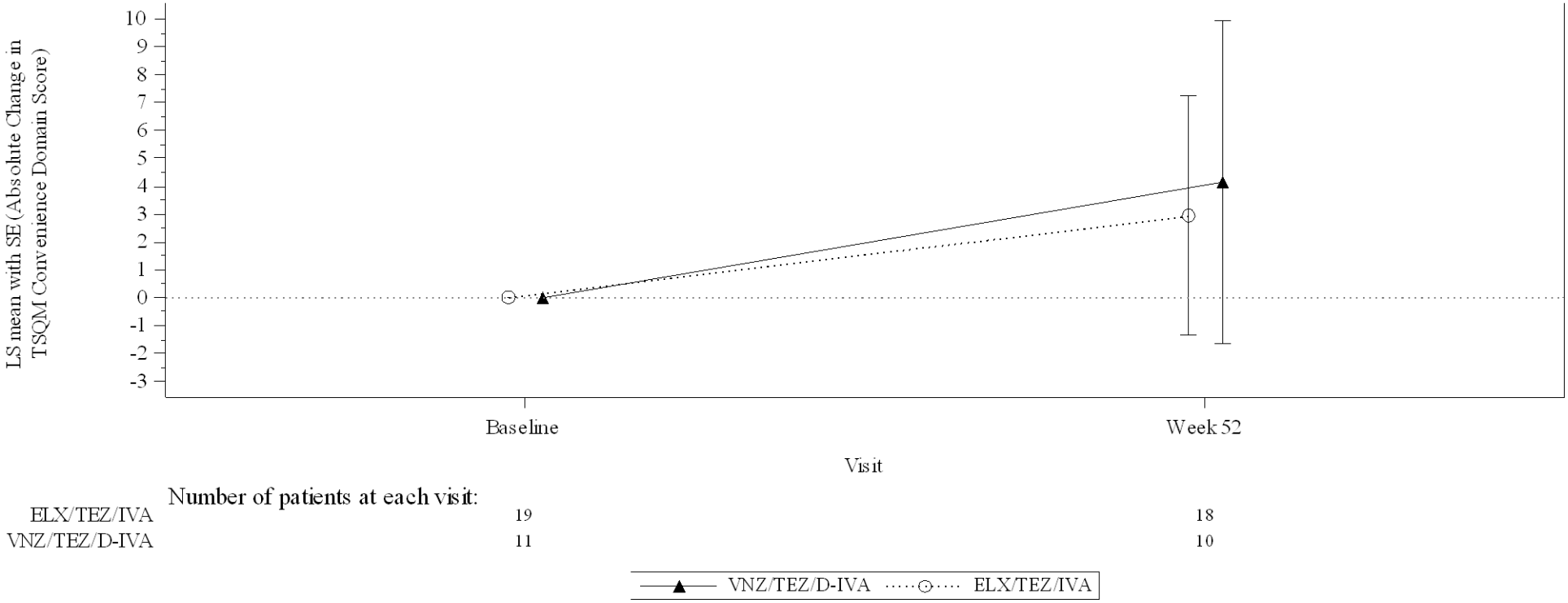
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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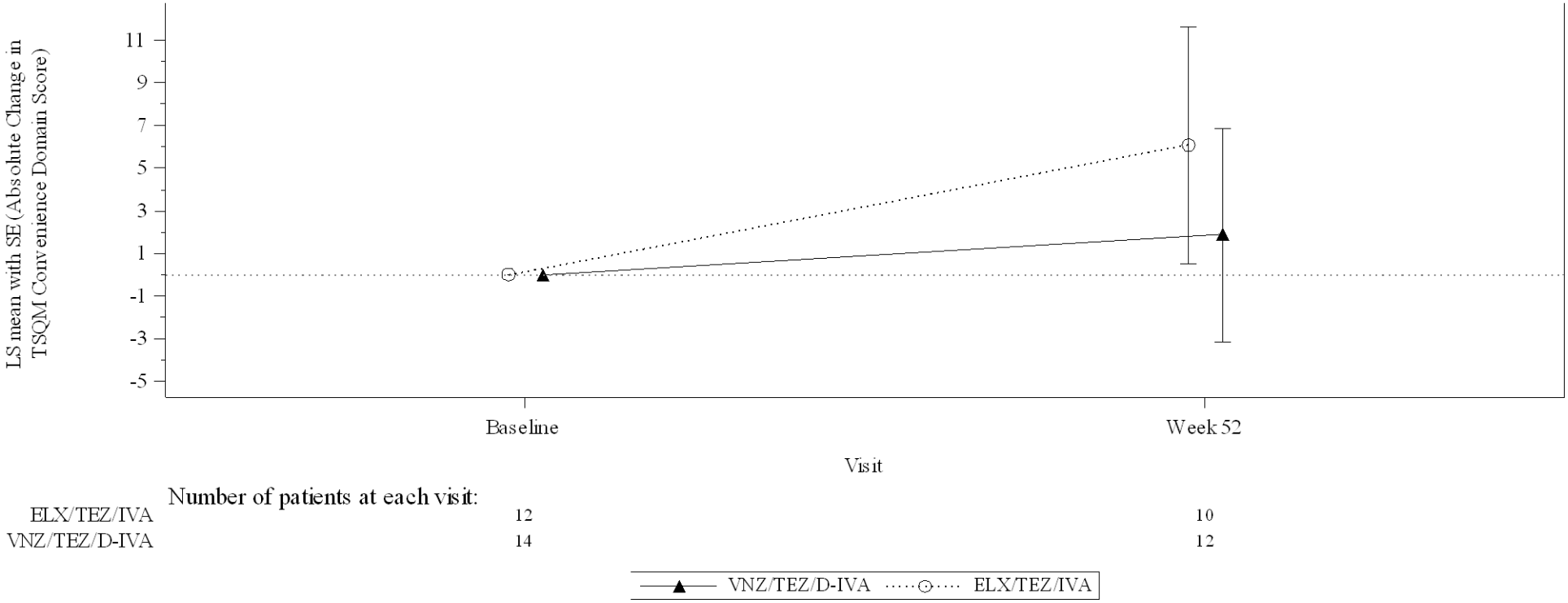
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = North America

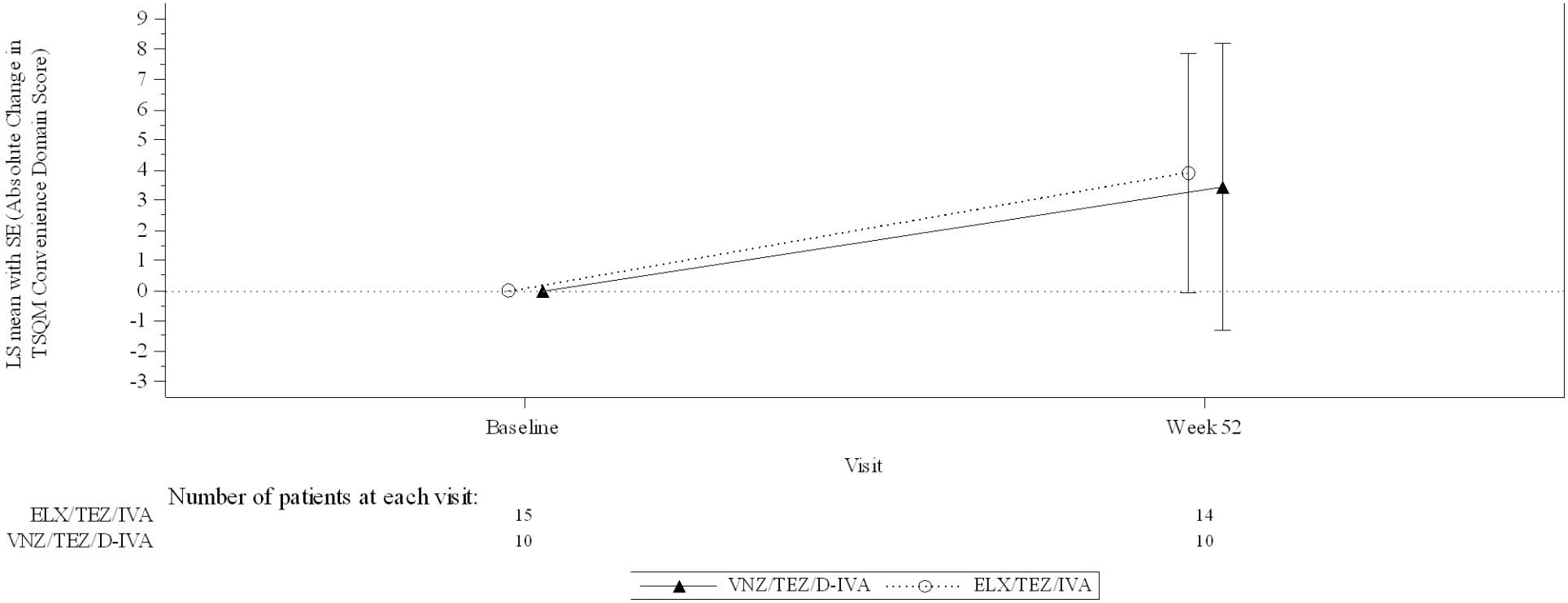

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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = Rest of World

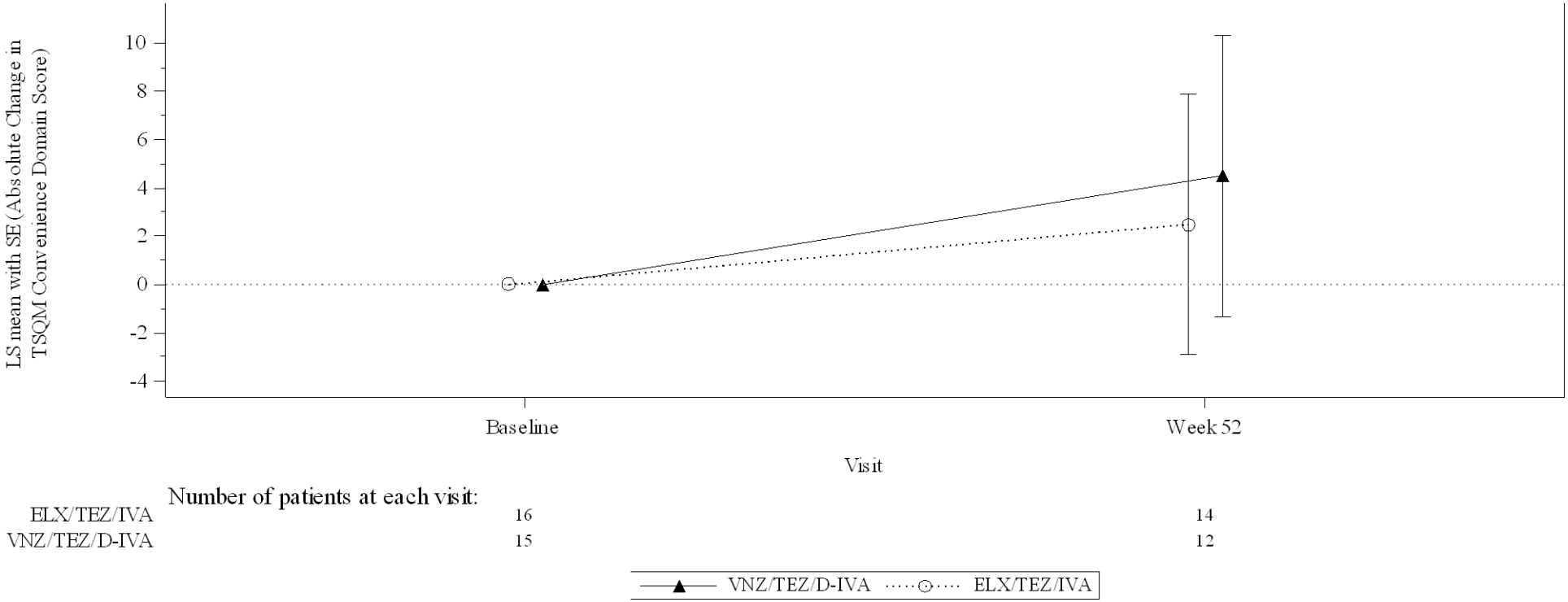

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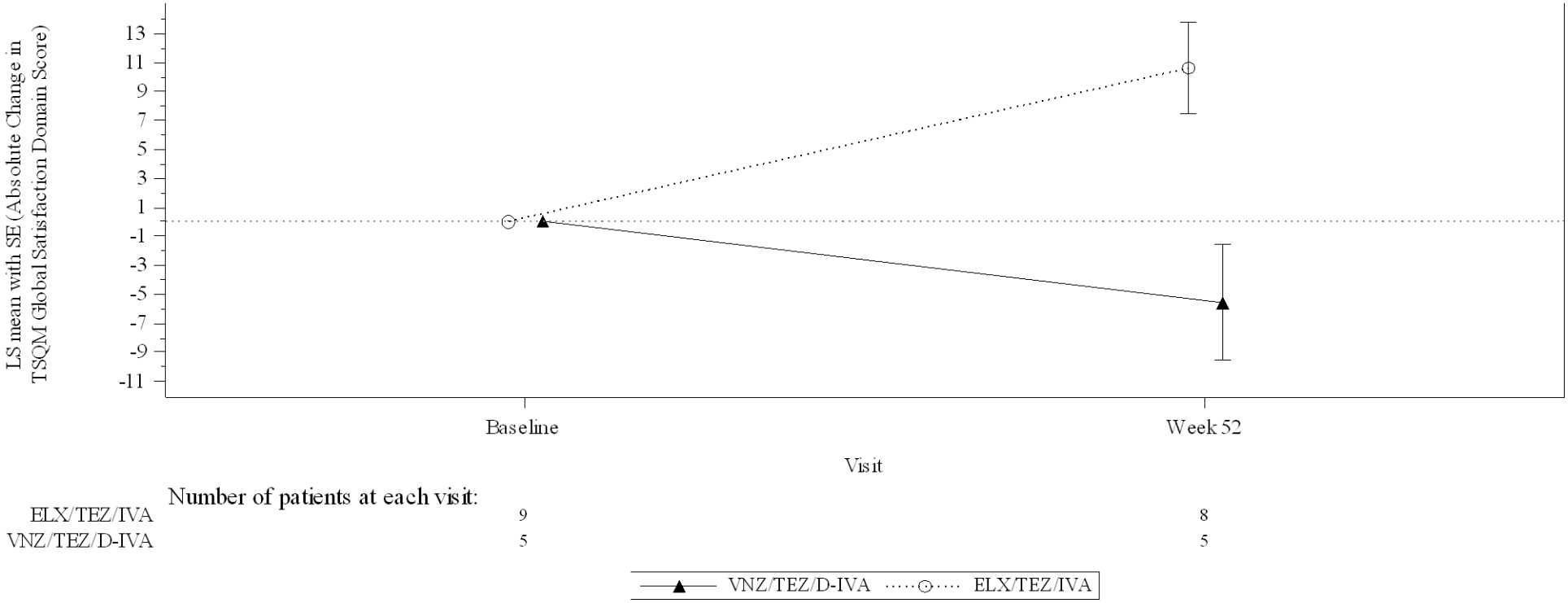
Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
ppFEV$_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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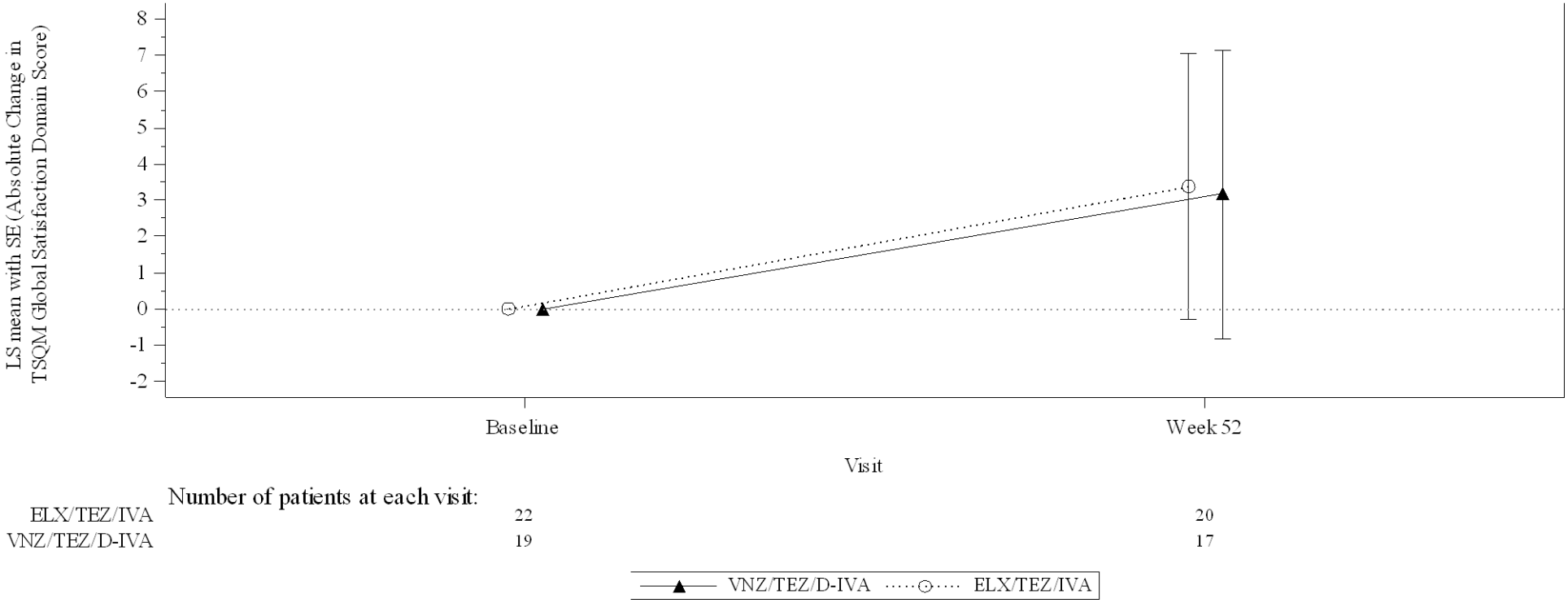
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
ppFEV$_1$ at baseline ≥70 %



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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Age at screening <18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Age at screening ≥18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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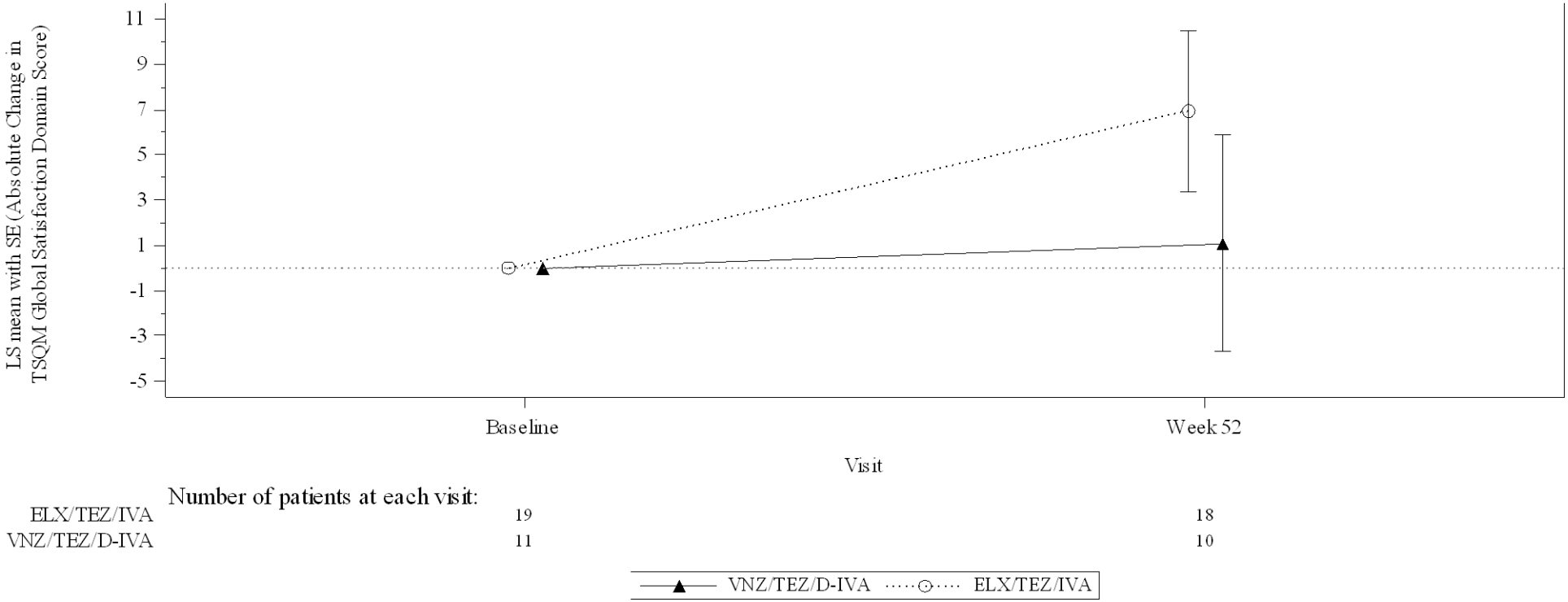
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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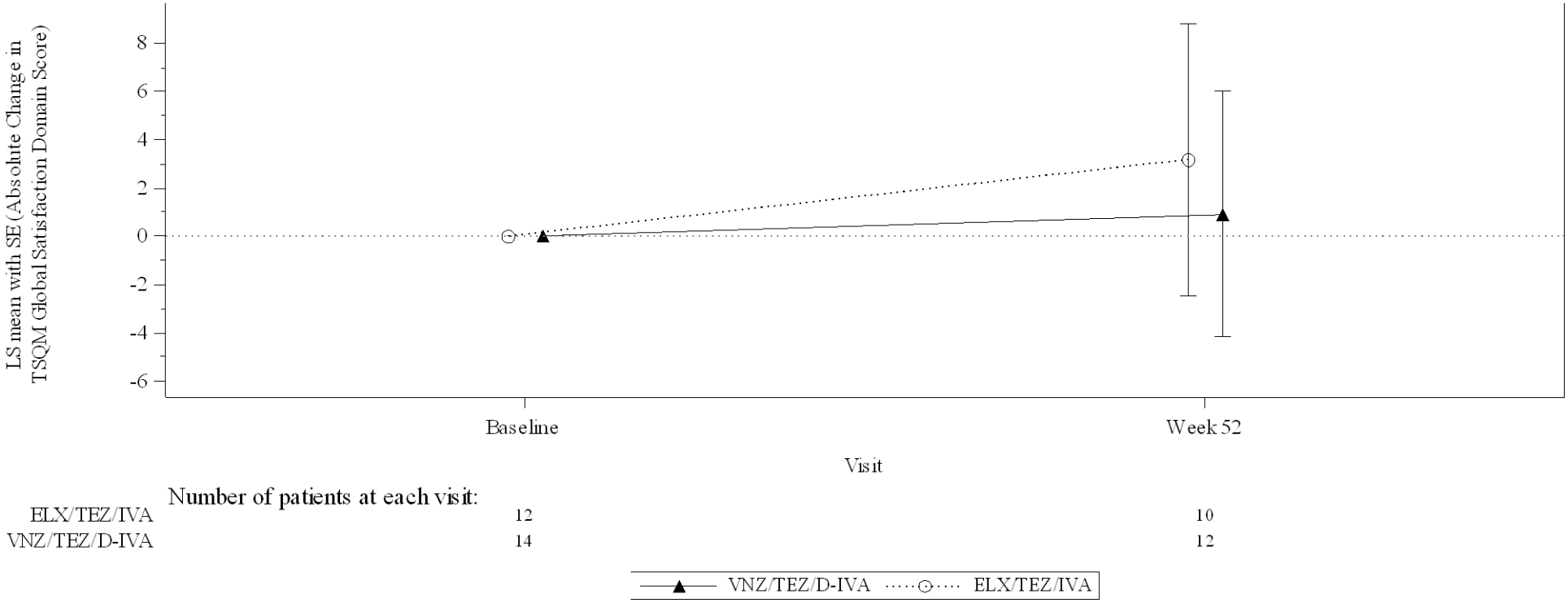
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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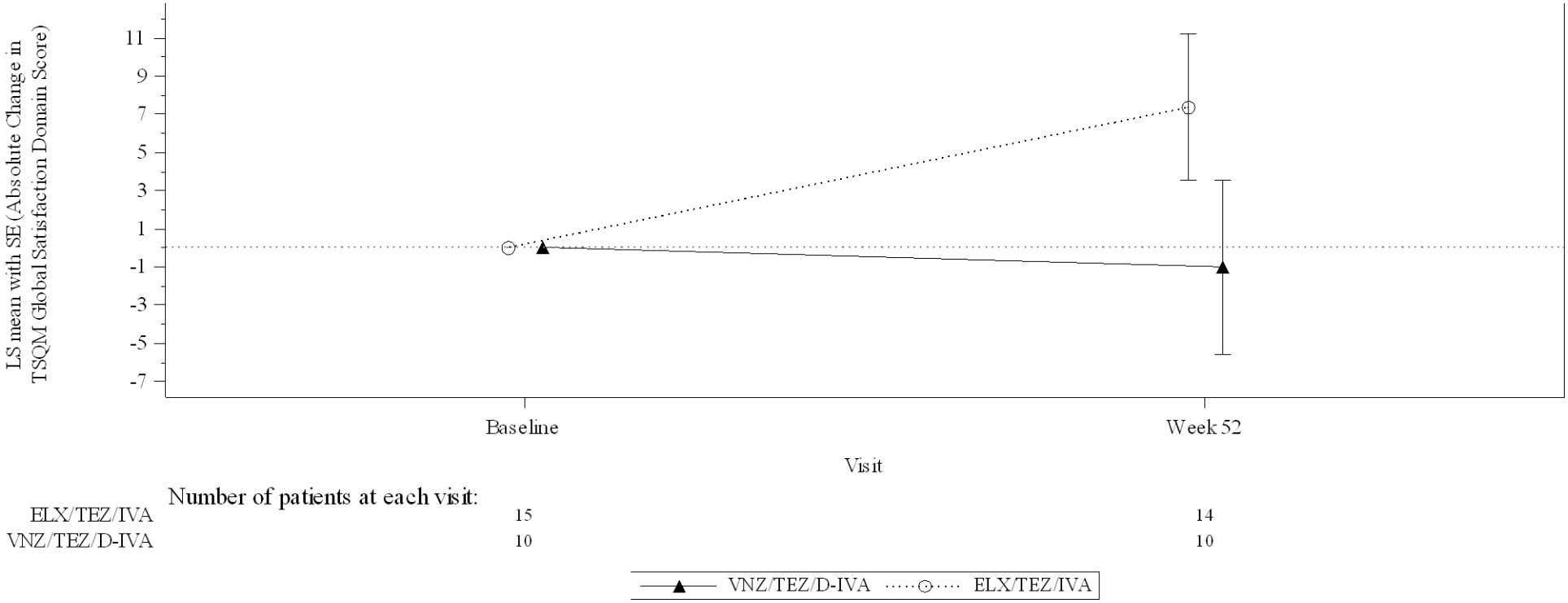
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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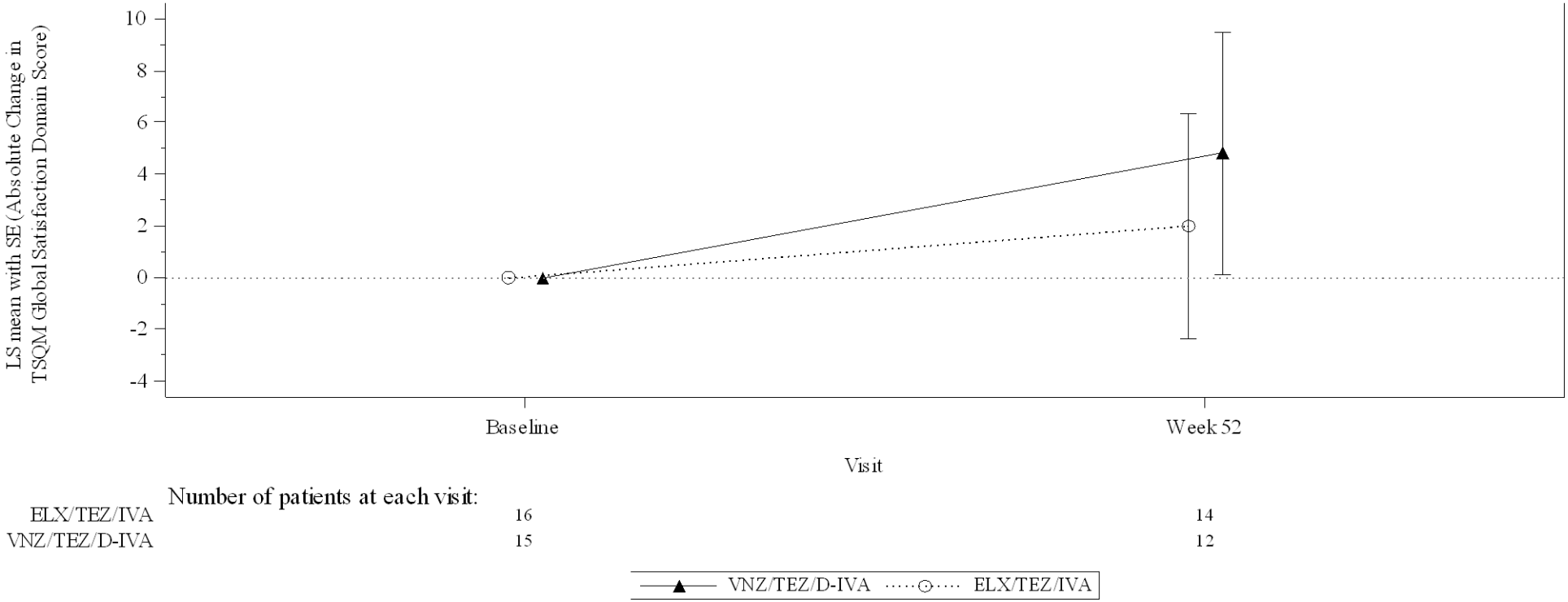
Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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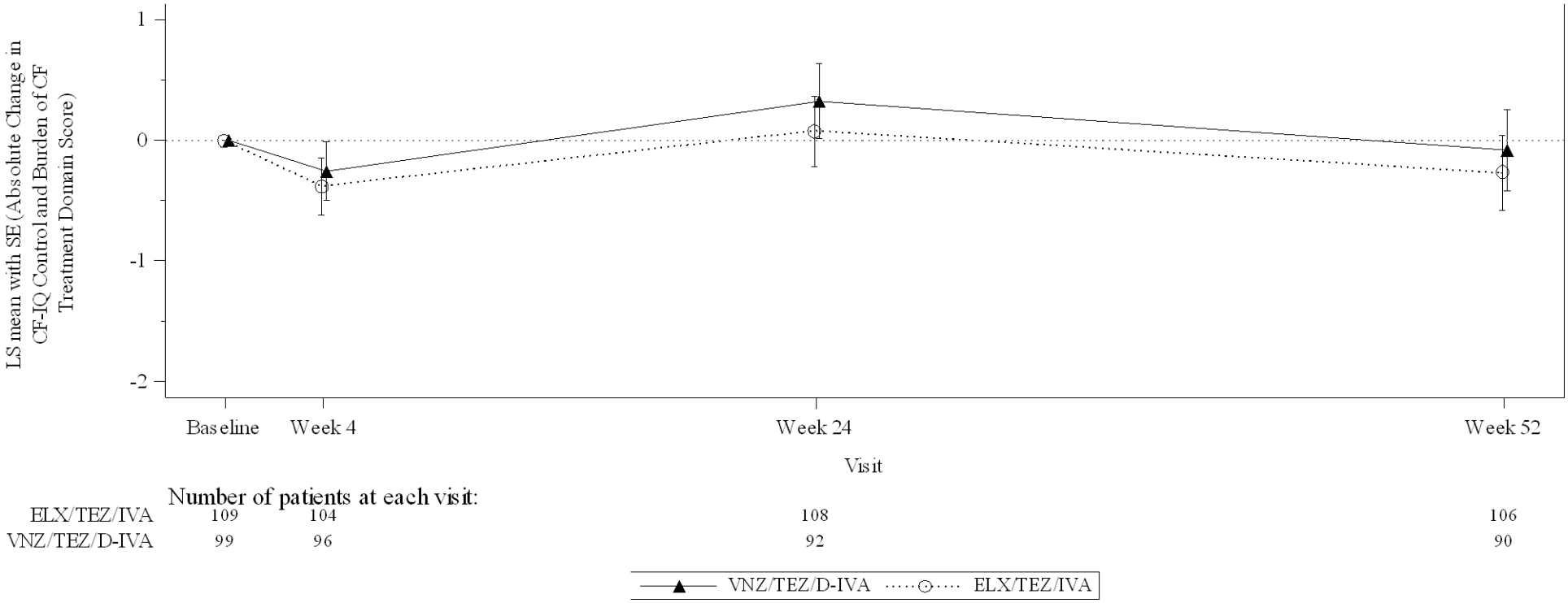
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-tsqm-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
ppFEV$_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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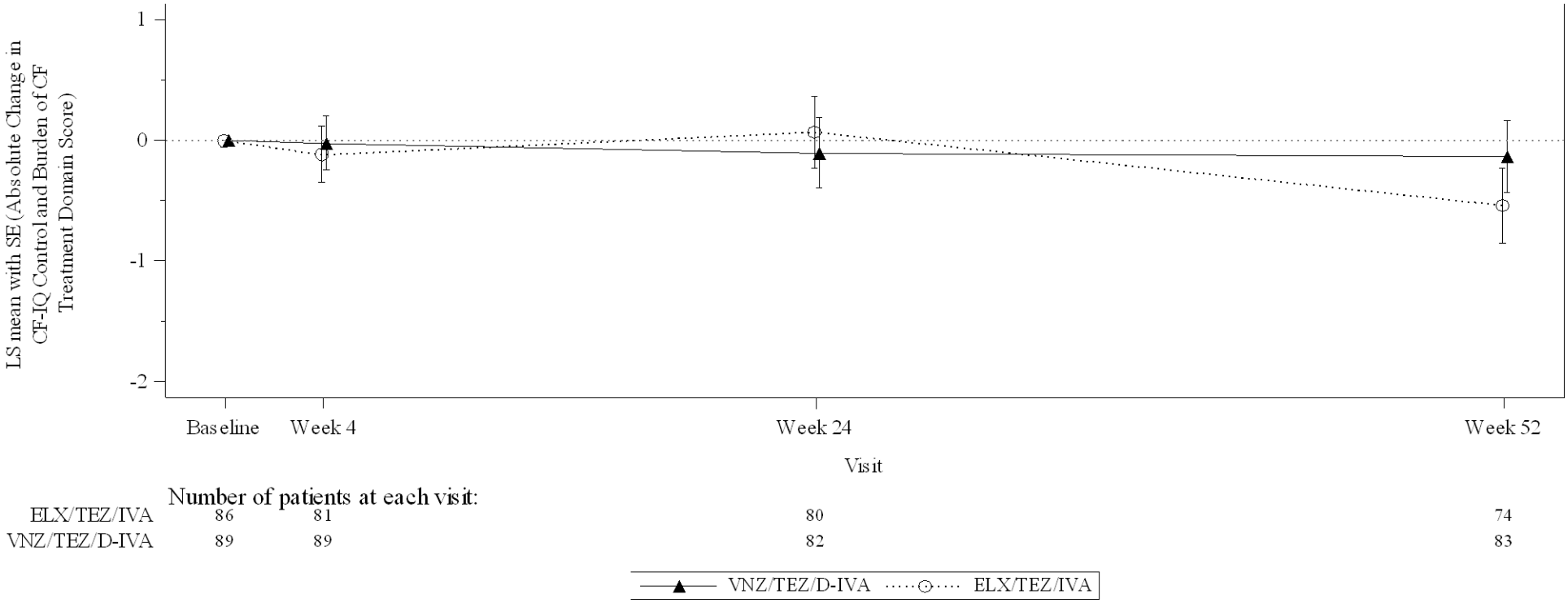
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
ppFEV$_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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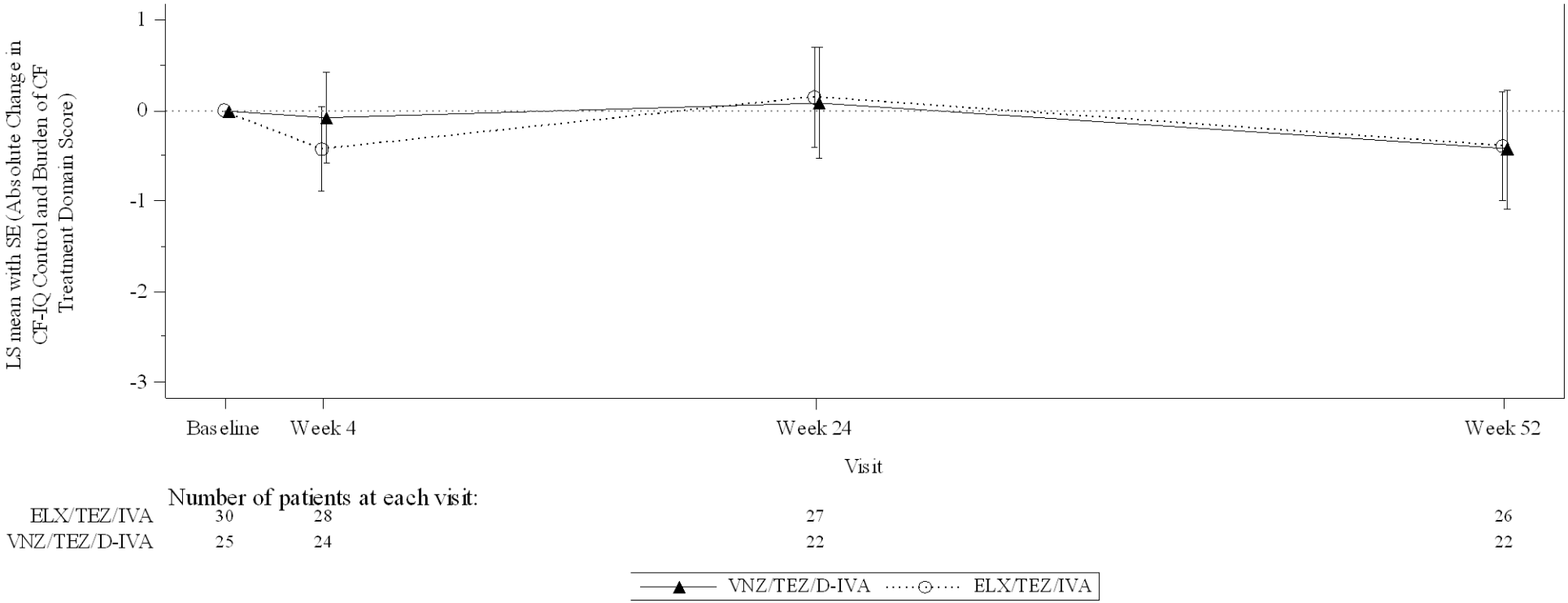
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening <18 years



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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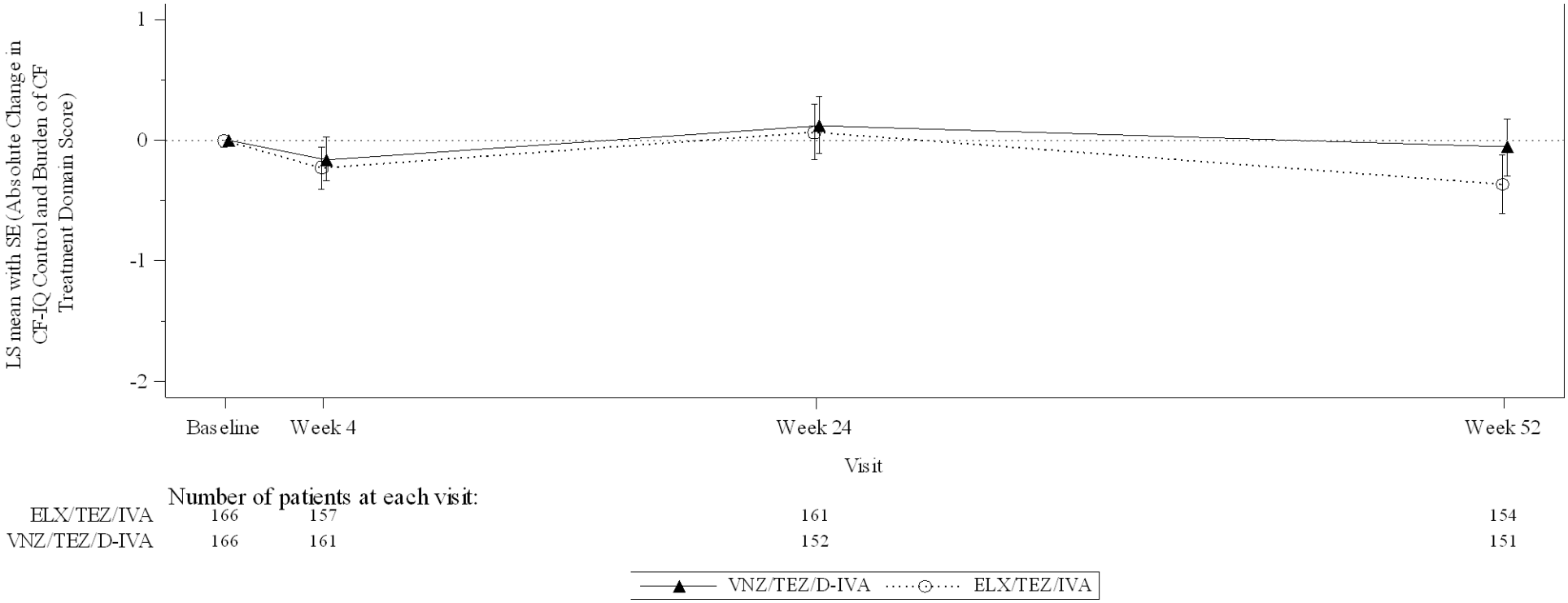
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening ≥18 years



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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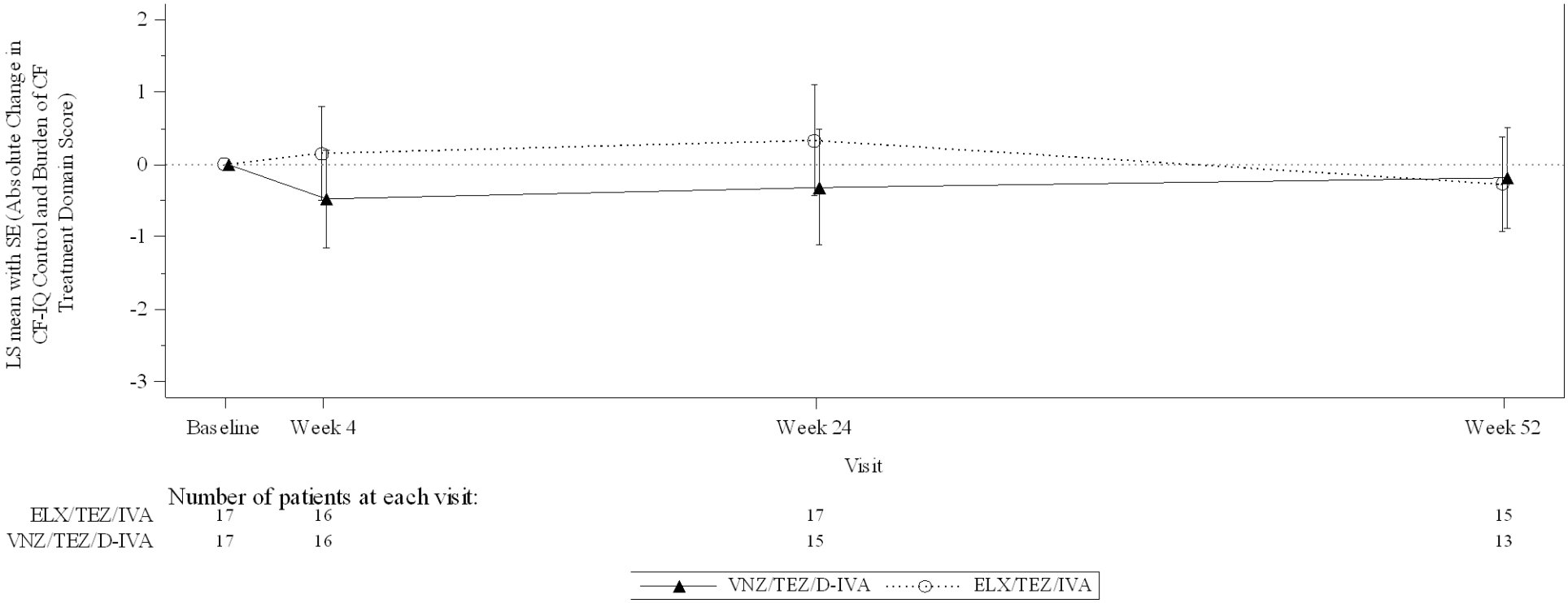
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline <30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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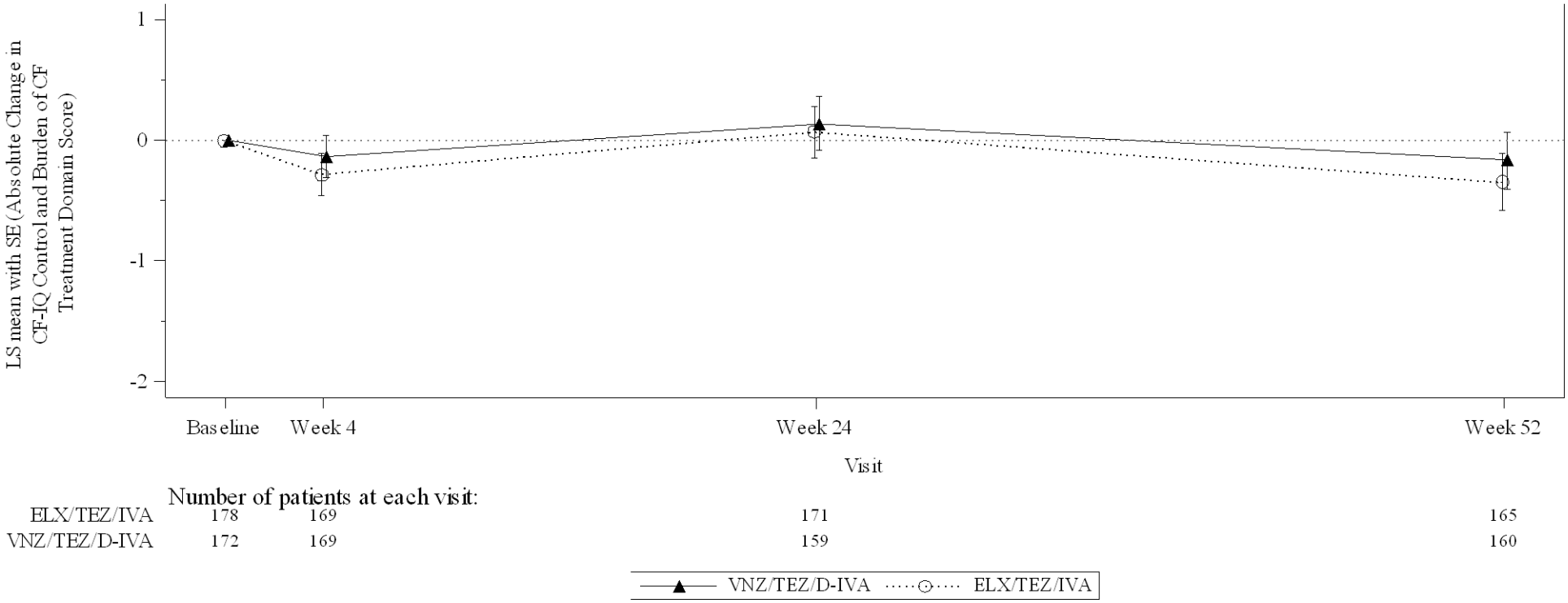
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline ≥30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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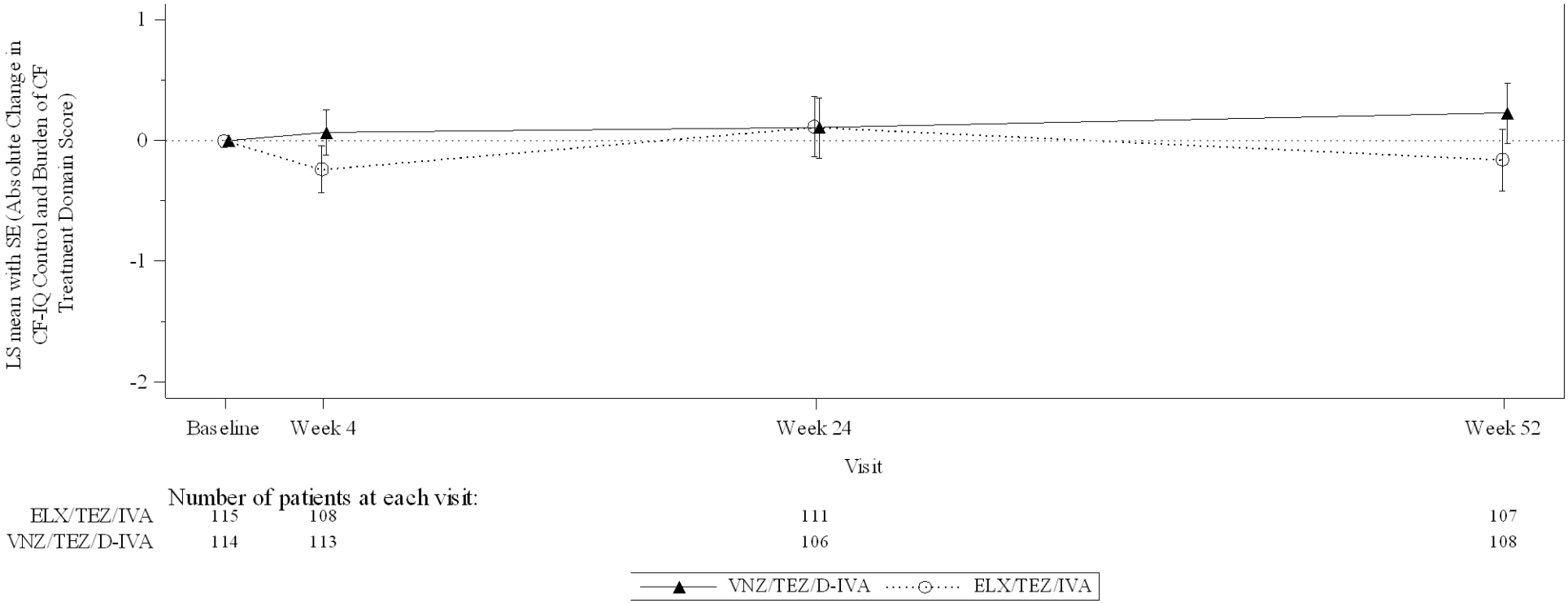
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Male



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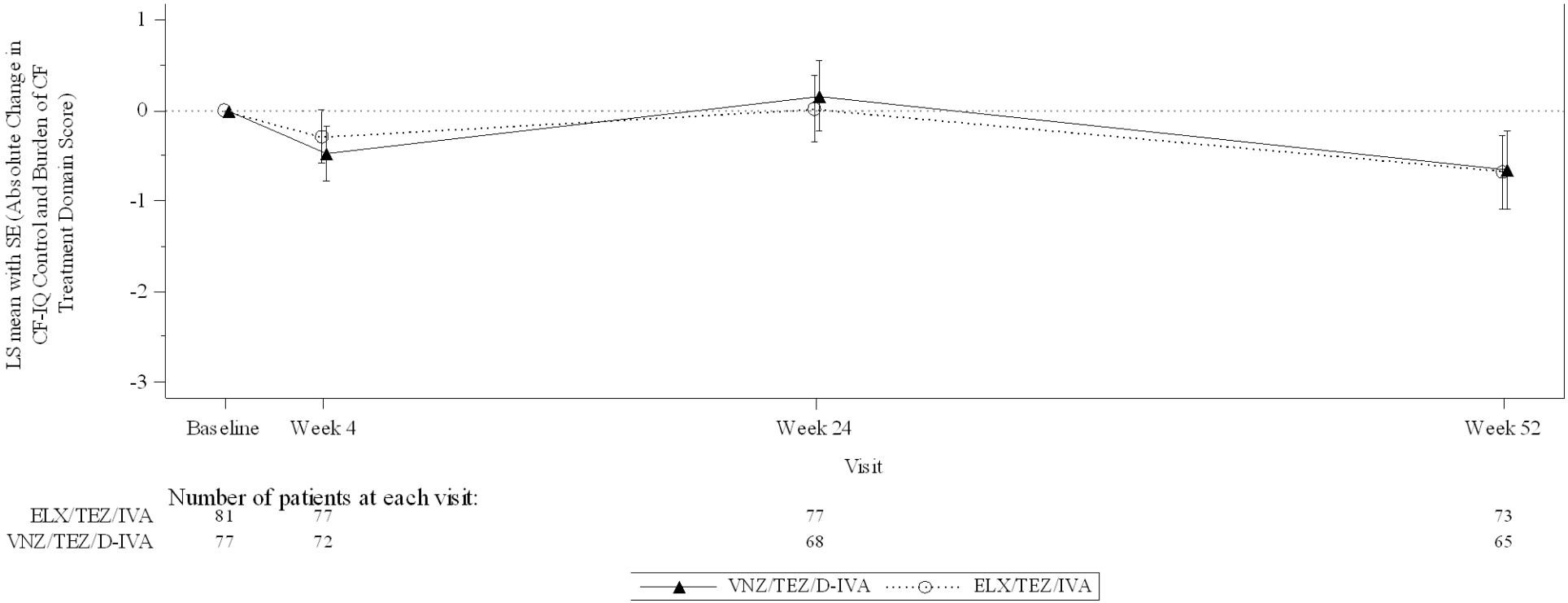
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Female



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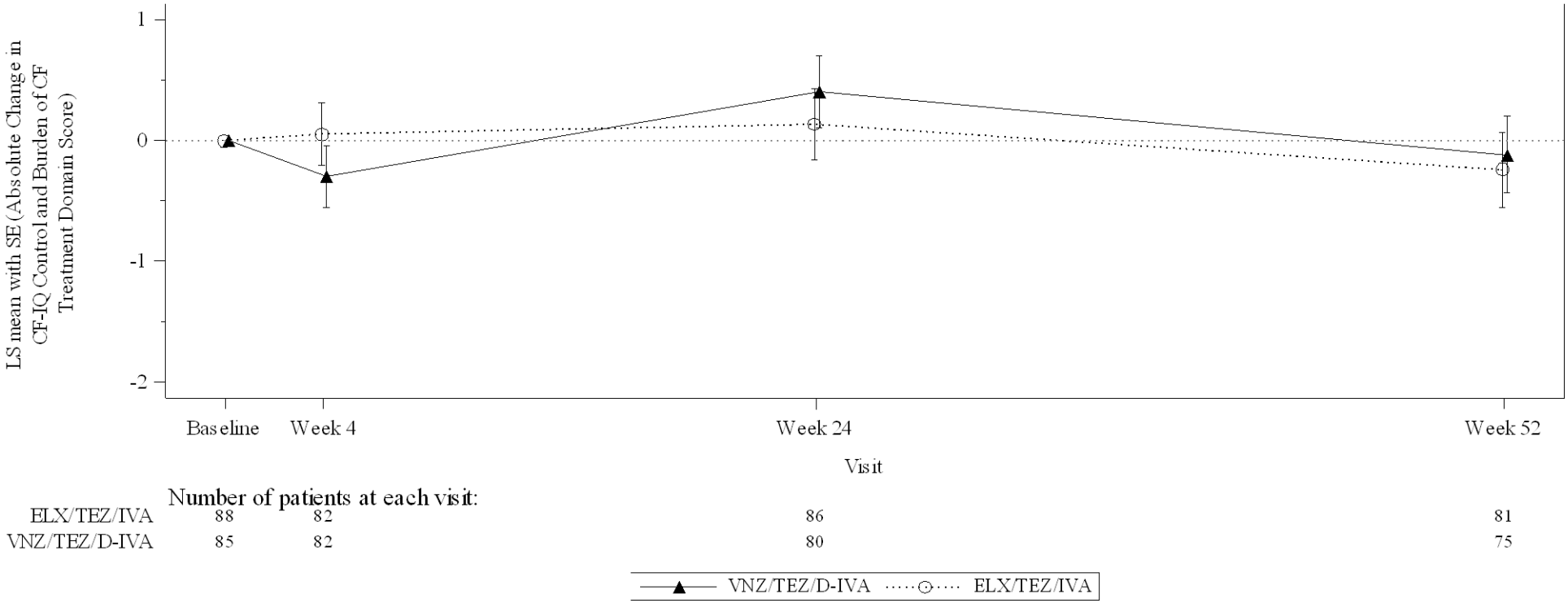
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = North America



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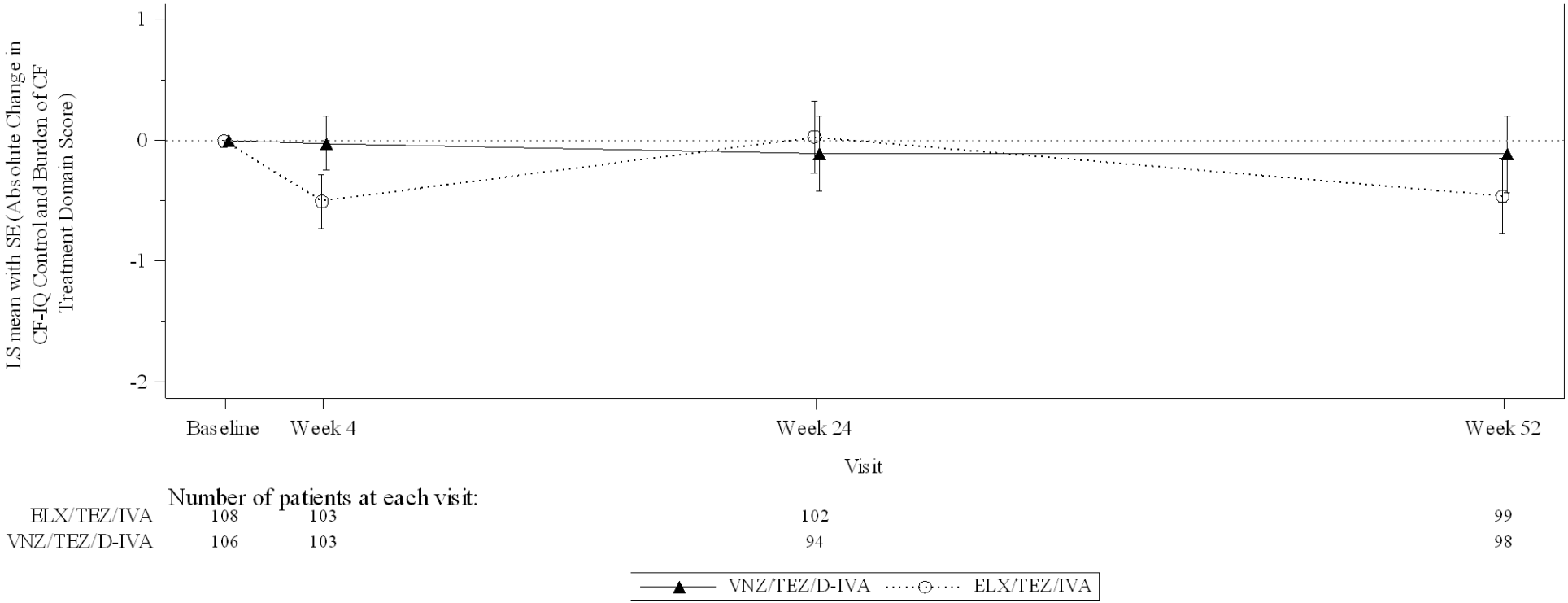
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = Rest of World



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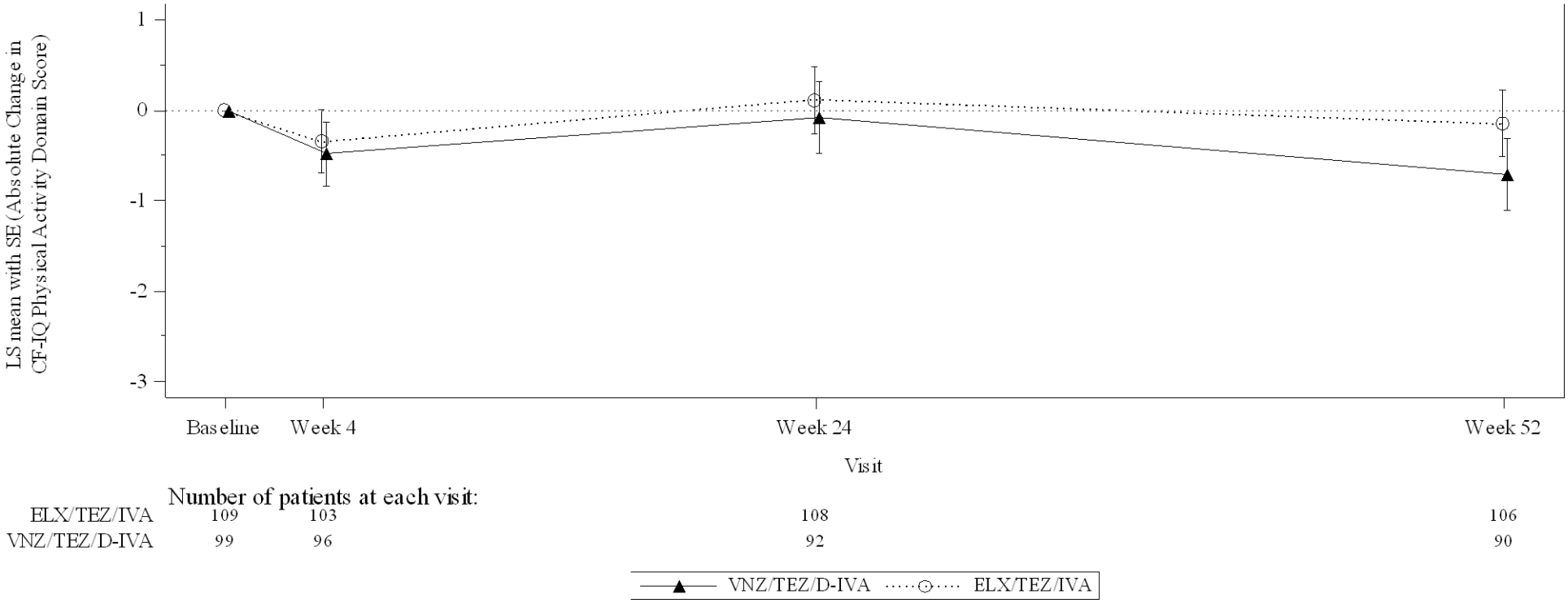
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
ppFEV$_1$ at baseline <70 %



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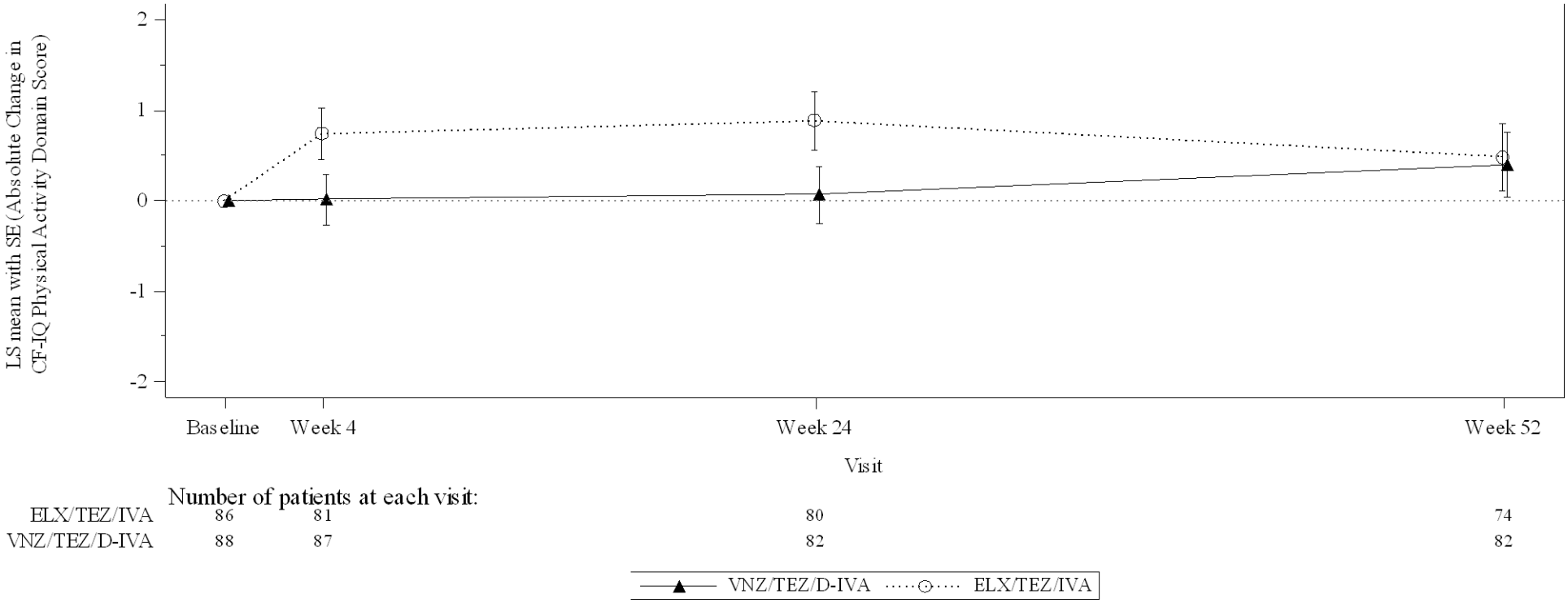
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
ppFEV$_1$ at baseline ≥70 %



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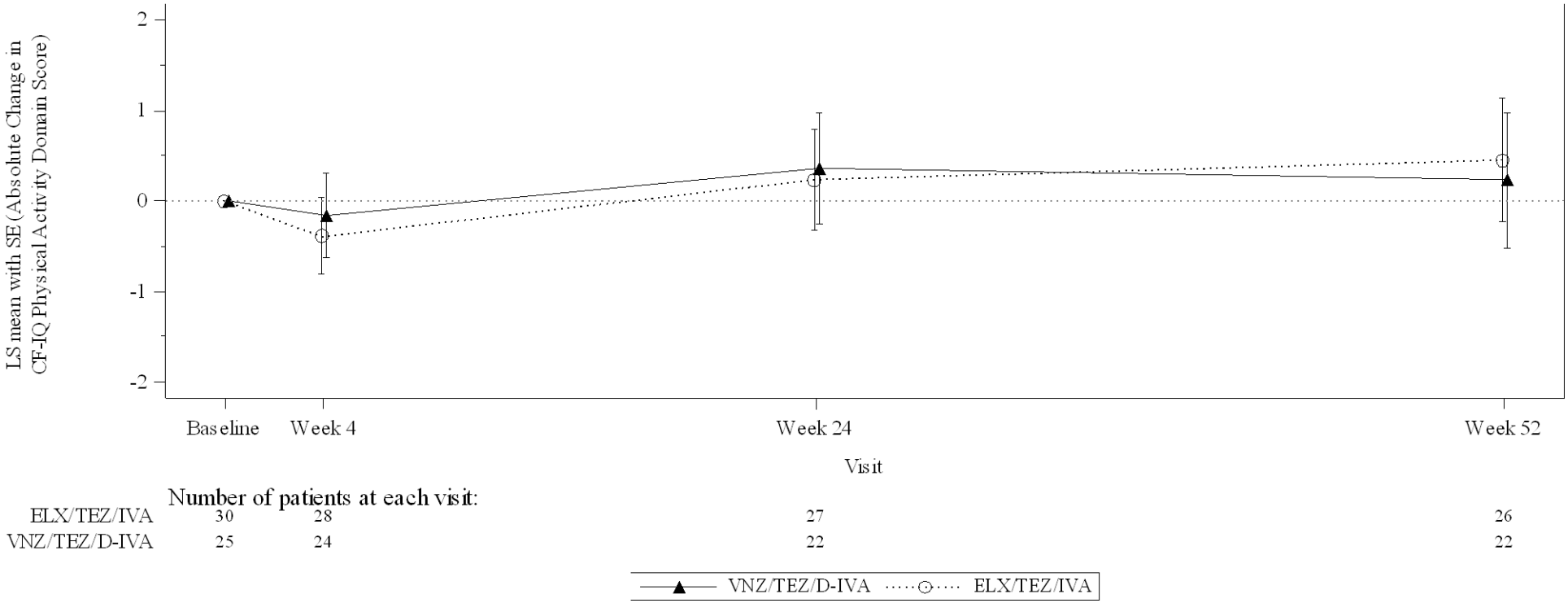
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
Age at screening <18 years



Number of patients at each visit:

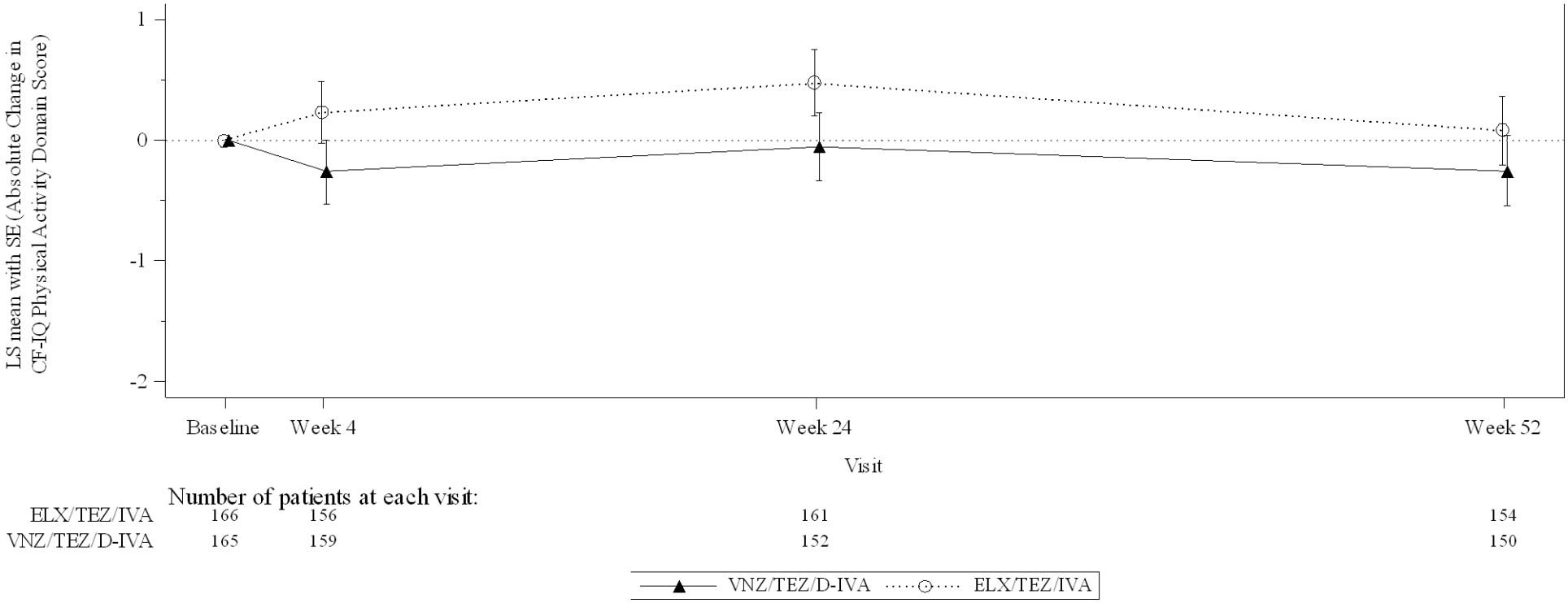
	Baseline	Week 4	Week 24	Week 52
ELX/TEZ/IVA	30	28	27	26
VNZ/TEZ/D-IVA	25	24	22	22

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
Age at screening ≥18 years



Number of patients at each visit:

ELX/TEZ/IVA	166	156	161	154
VNZ/TEZ/D-IVA	165	159	152	150

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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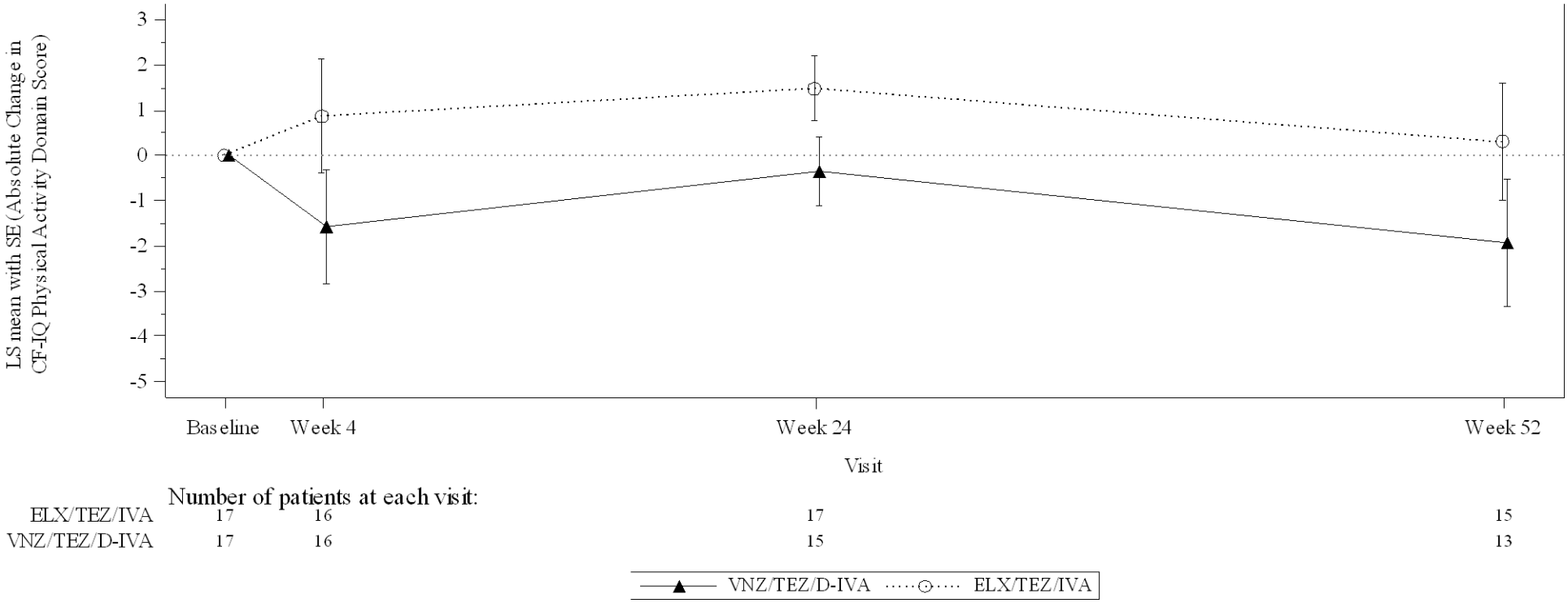
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
SwCl at baseline <30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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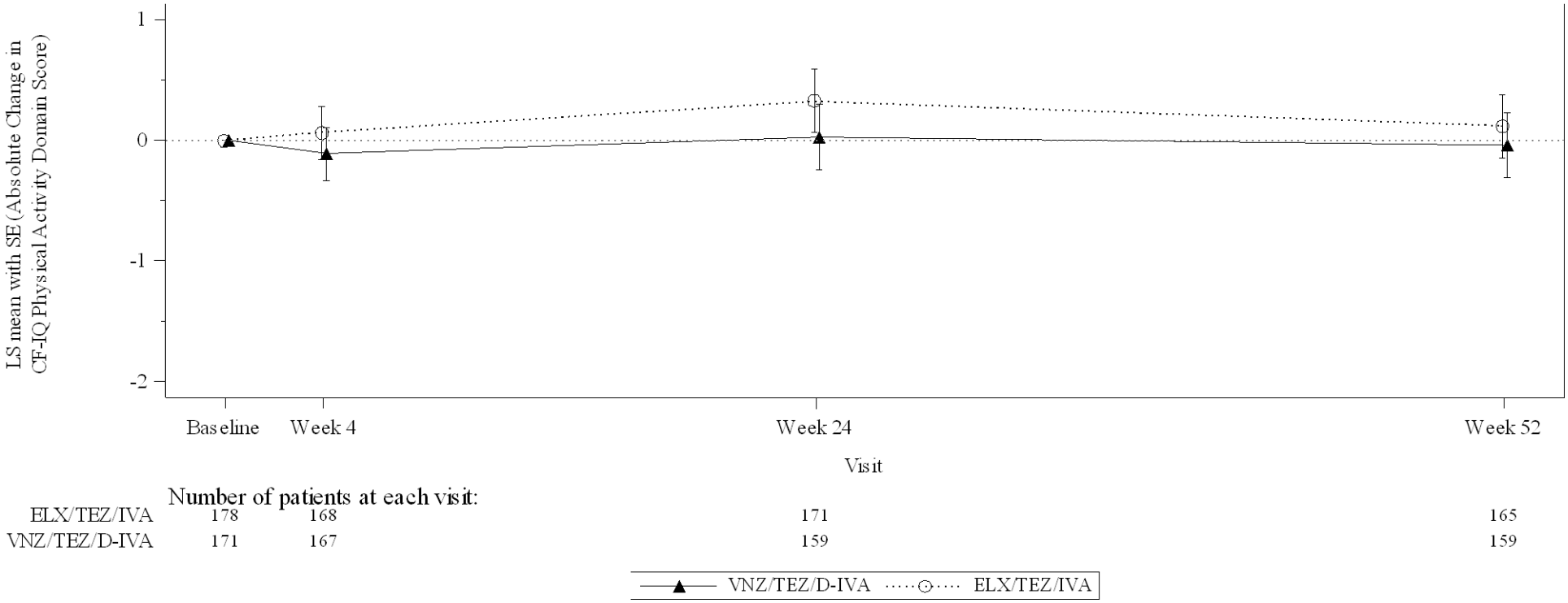
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
SwCl at baseline ≥30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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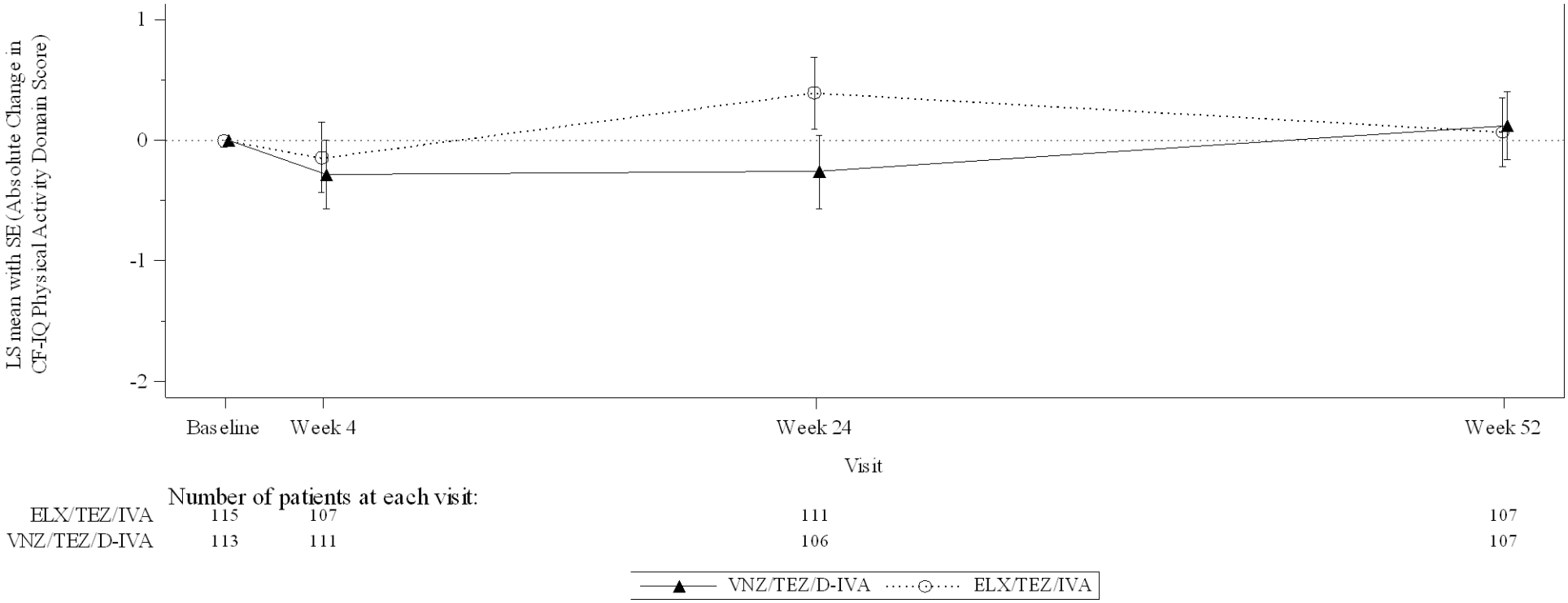
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
Sex = Male

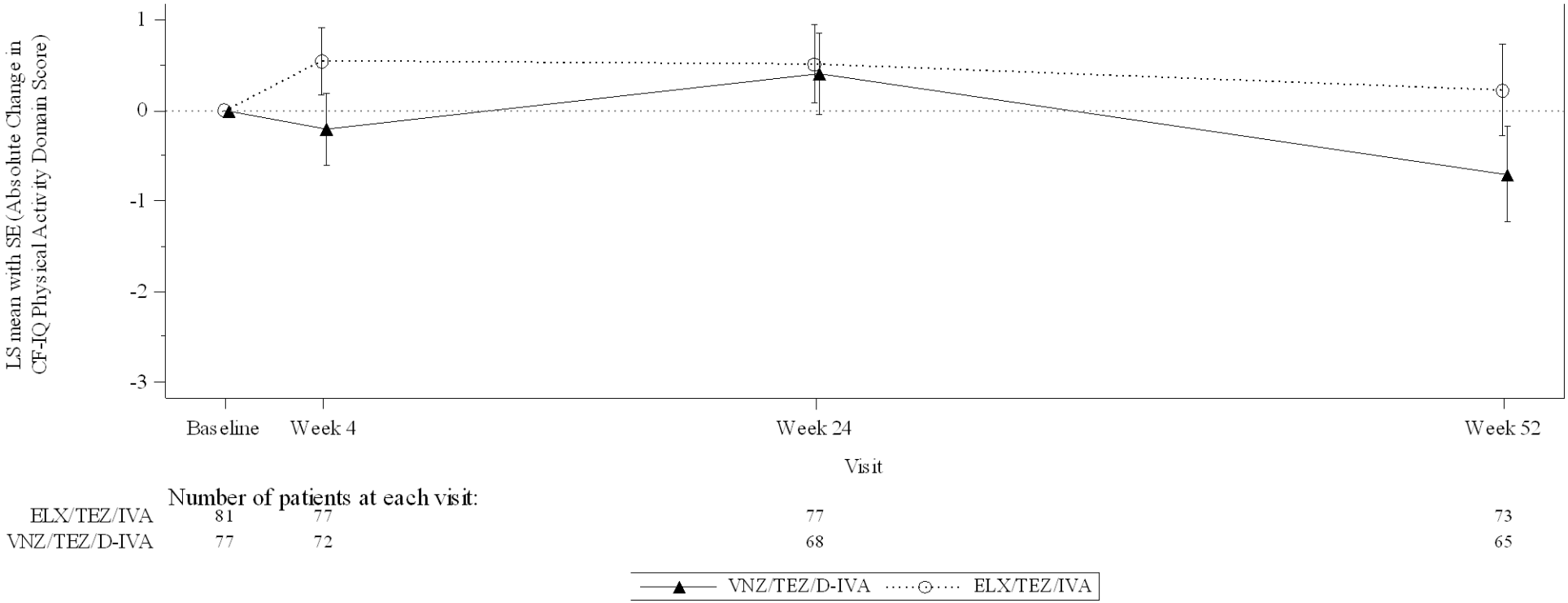


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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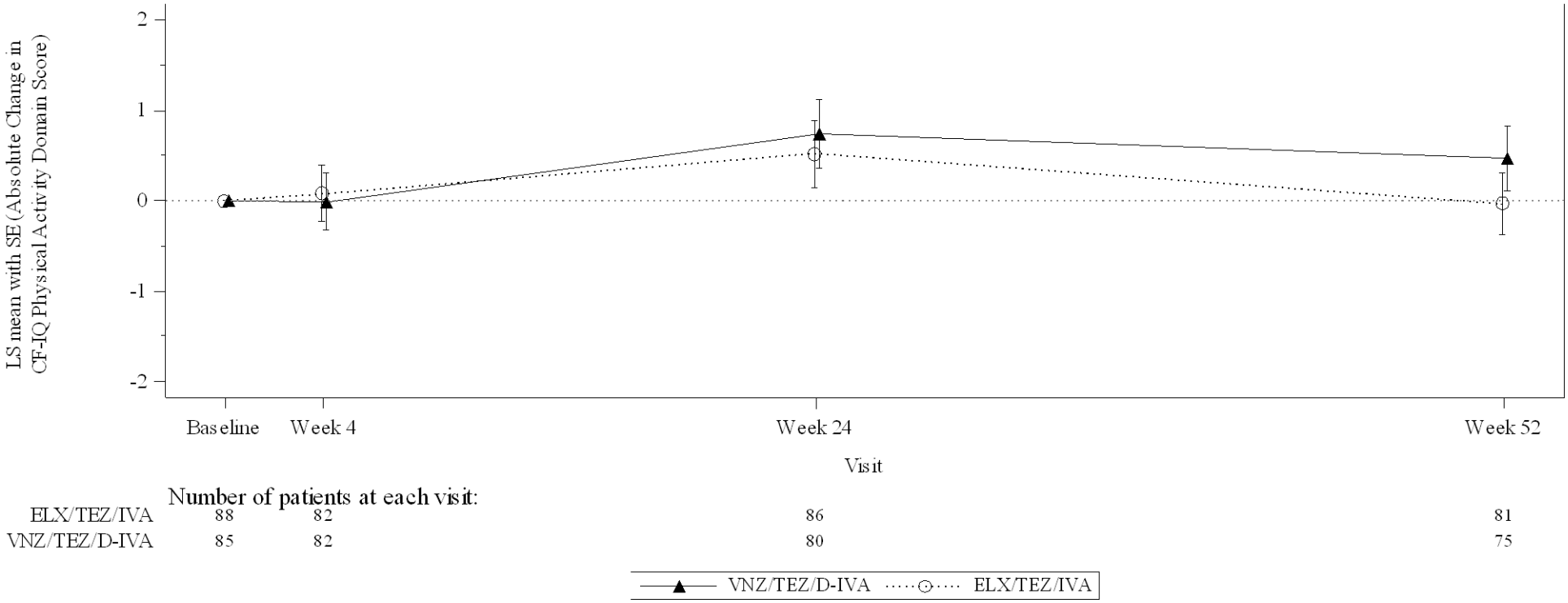
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
Region = North America



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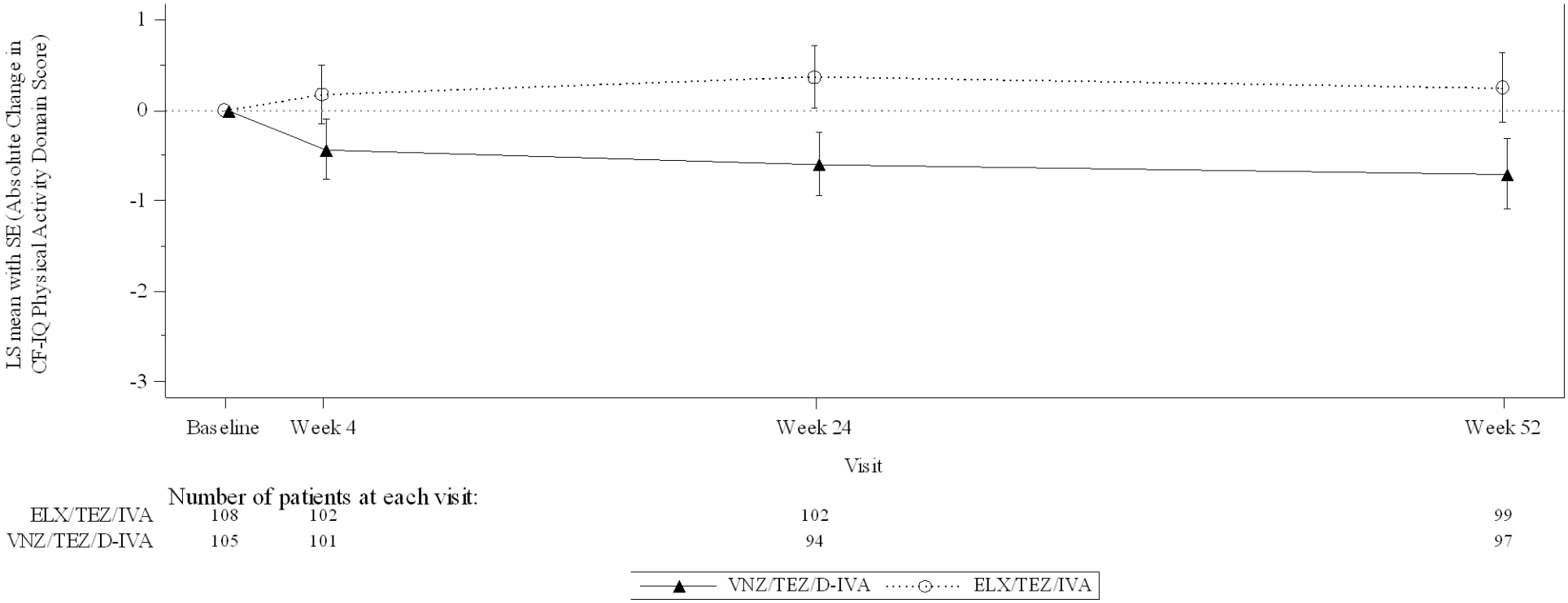
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
Region = Rest of World



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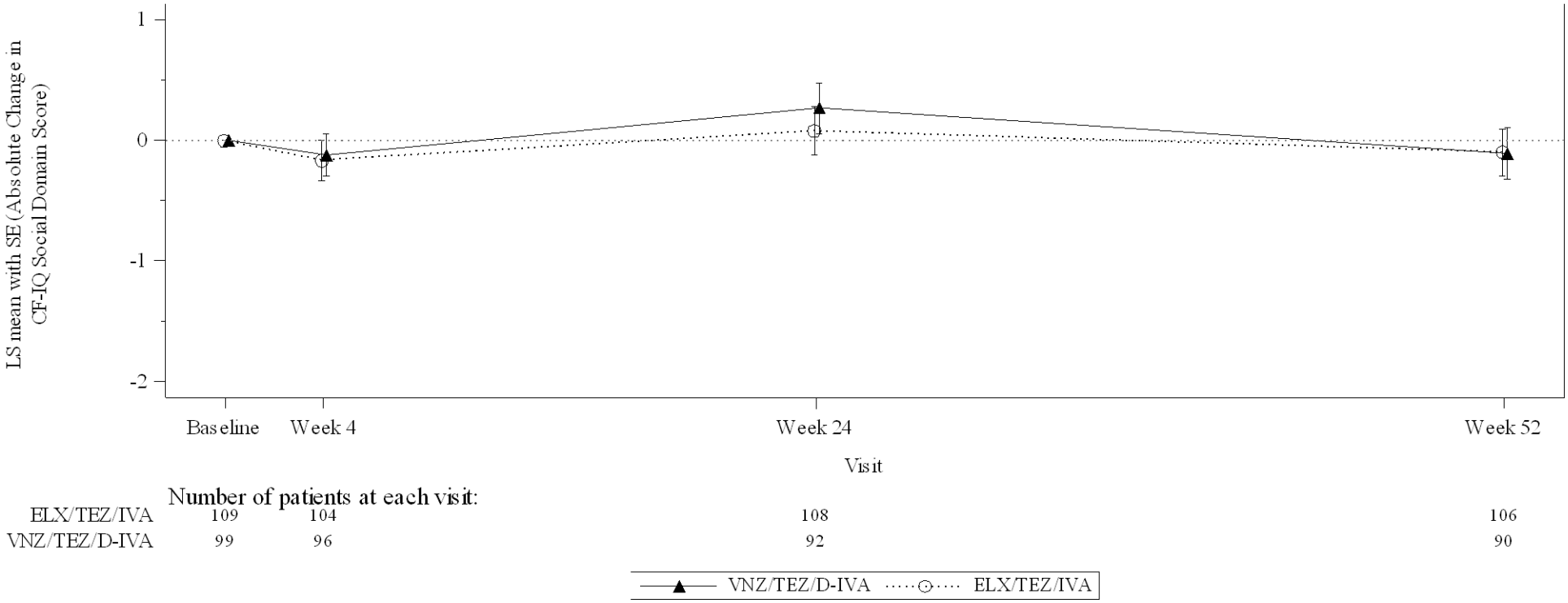
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
ppFEV$_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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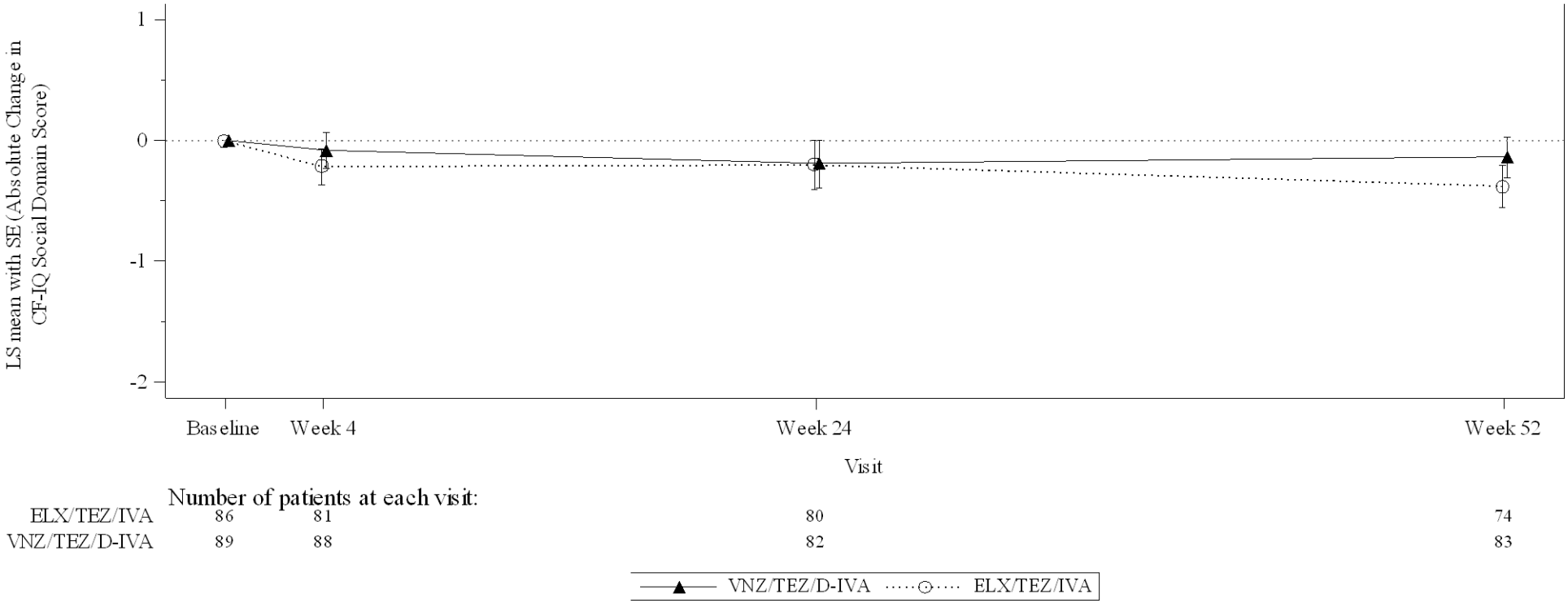
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
ppFEV$_1$ at baseline ≥70 %



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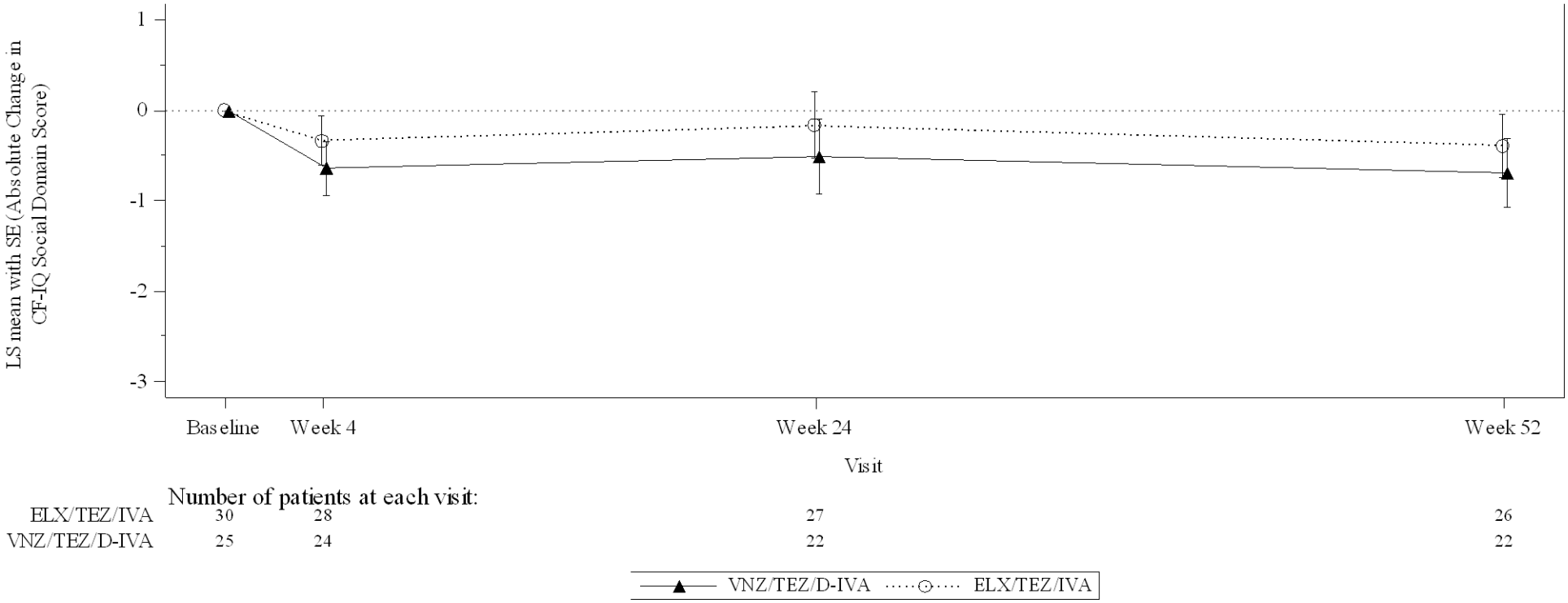
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
Age at screening <18 years



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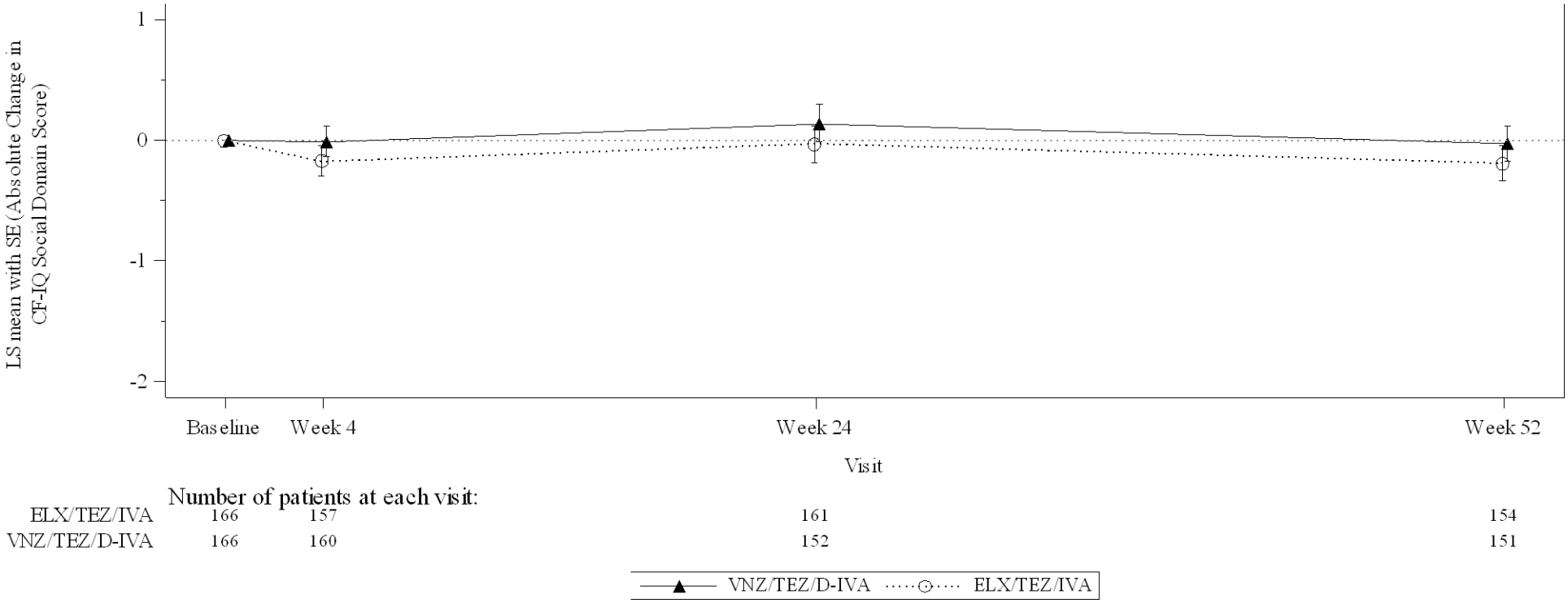
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
Age at screening ≥18 years



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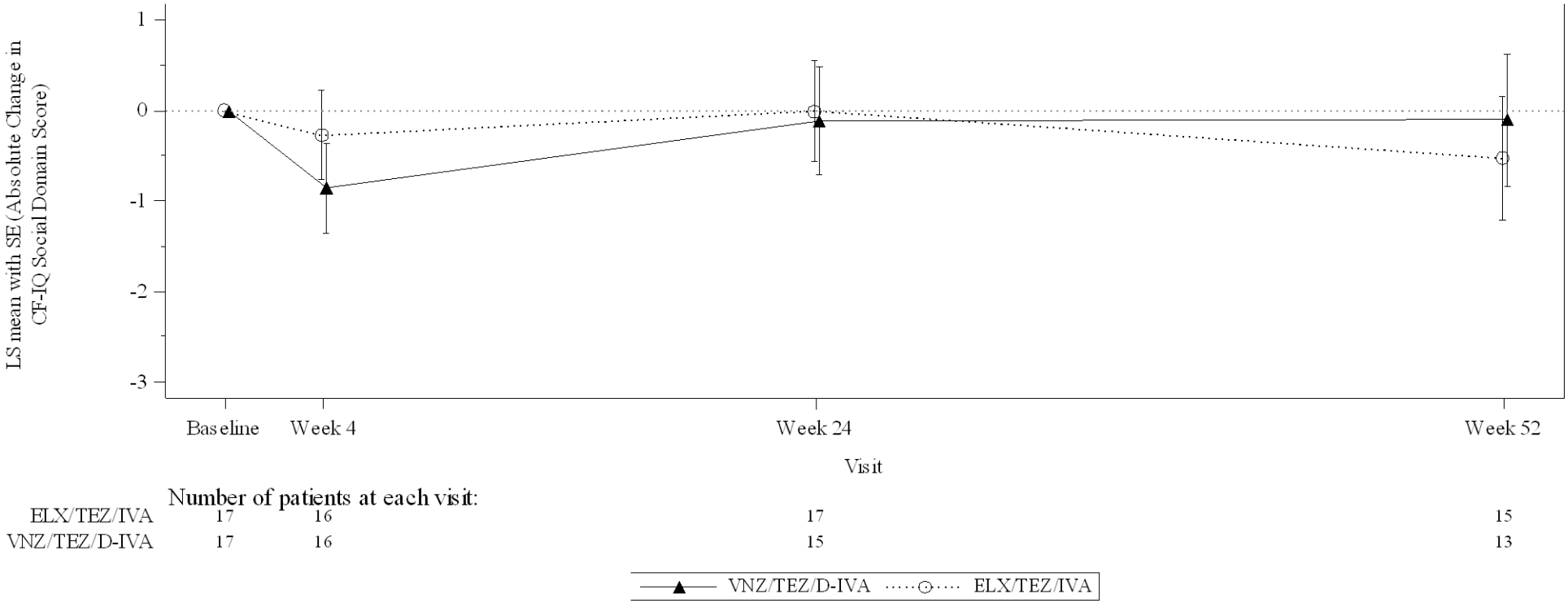
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
SwCl at baseline <30 mmol/L



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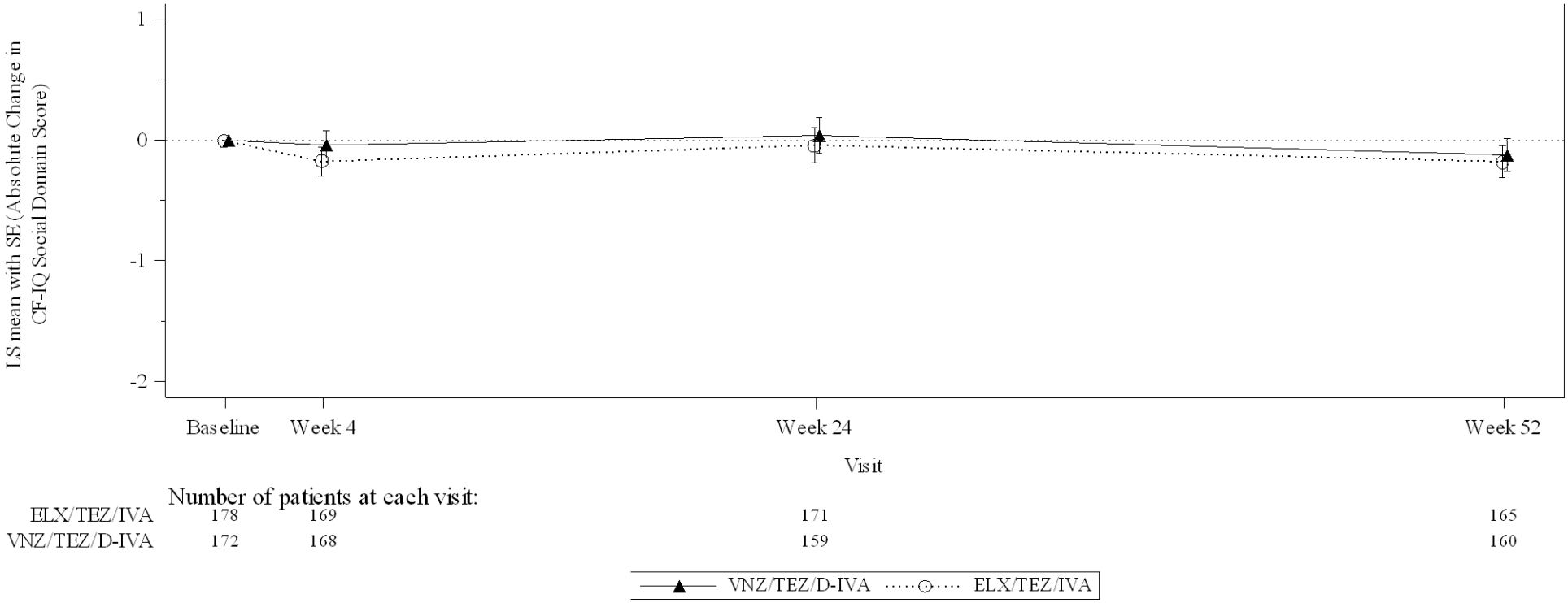
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
SwCl at baseline ≥30 mmol/L



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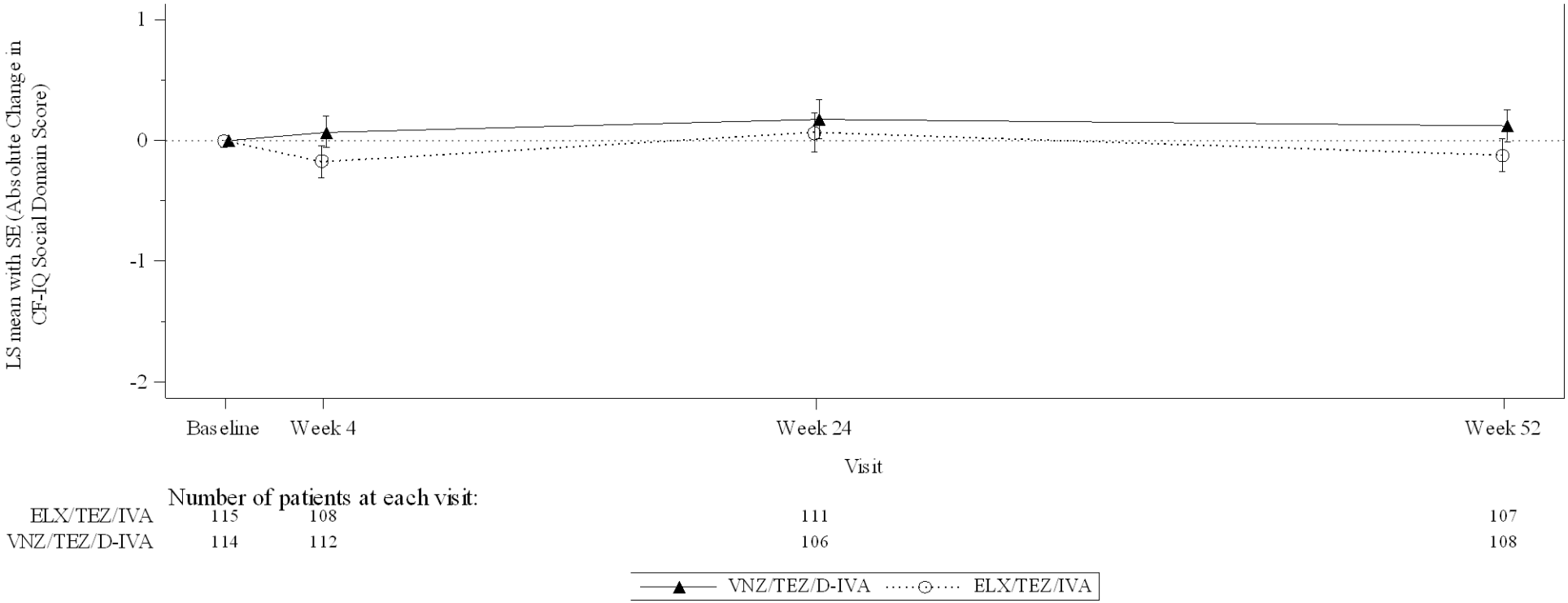
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
Sex = Male



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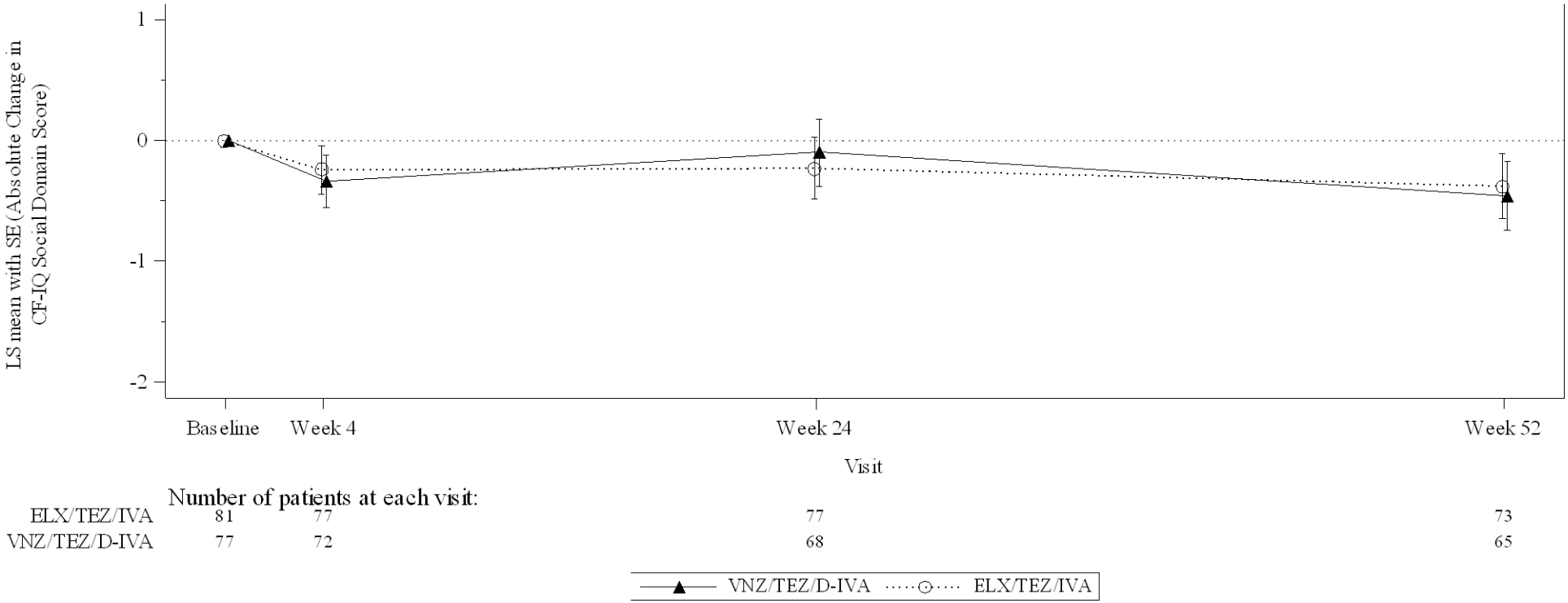
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
Sex = Female



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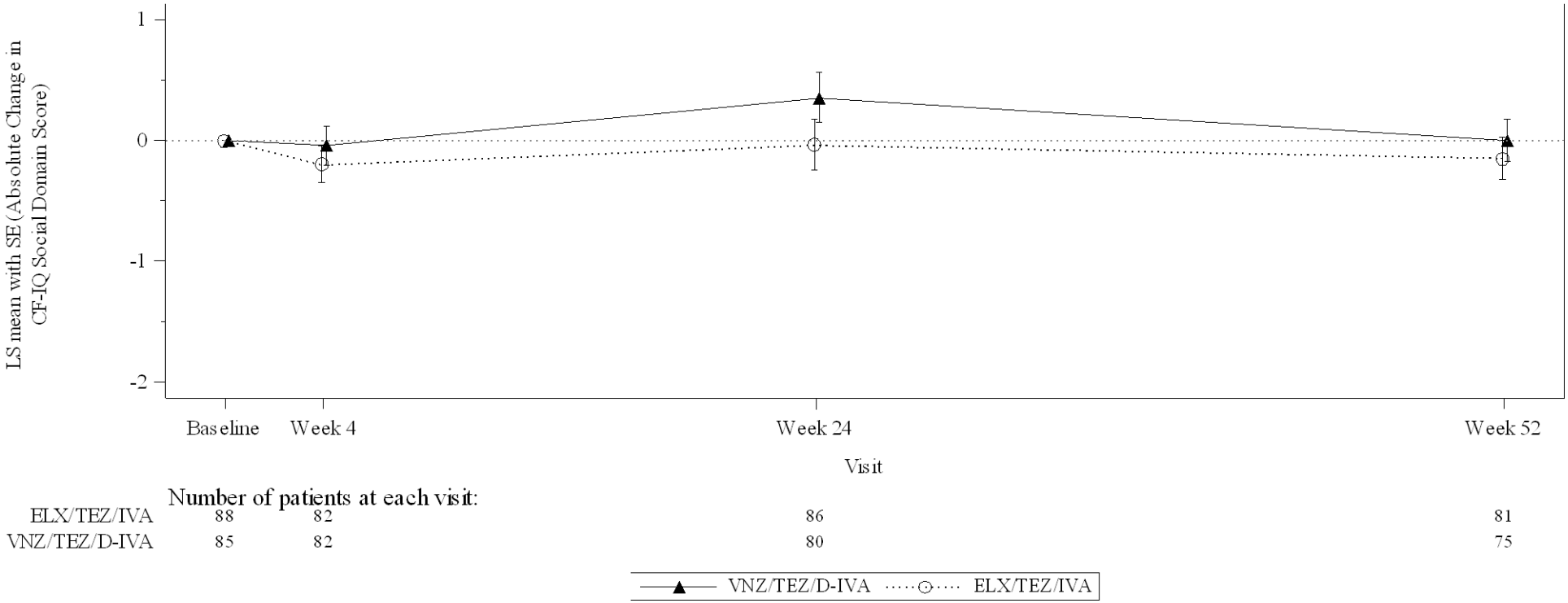
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
Region = North America



Number of patients at each visit:

	Baseline	Week 4	Week 24	Week 52
ELX/TEZ/IVA	88	82	86	81
VNZ/TEZ/D-IVA	85	82	80	75

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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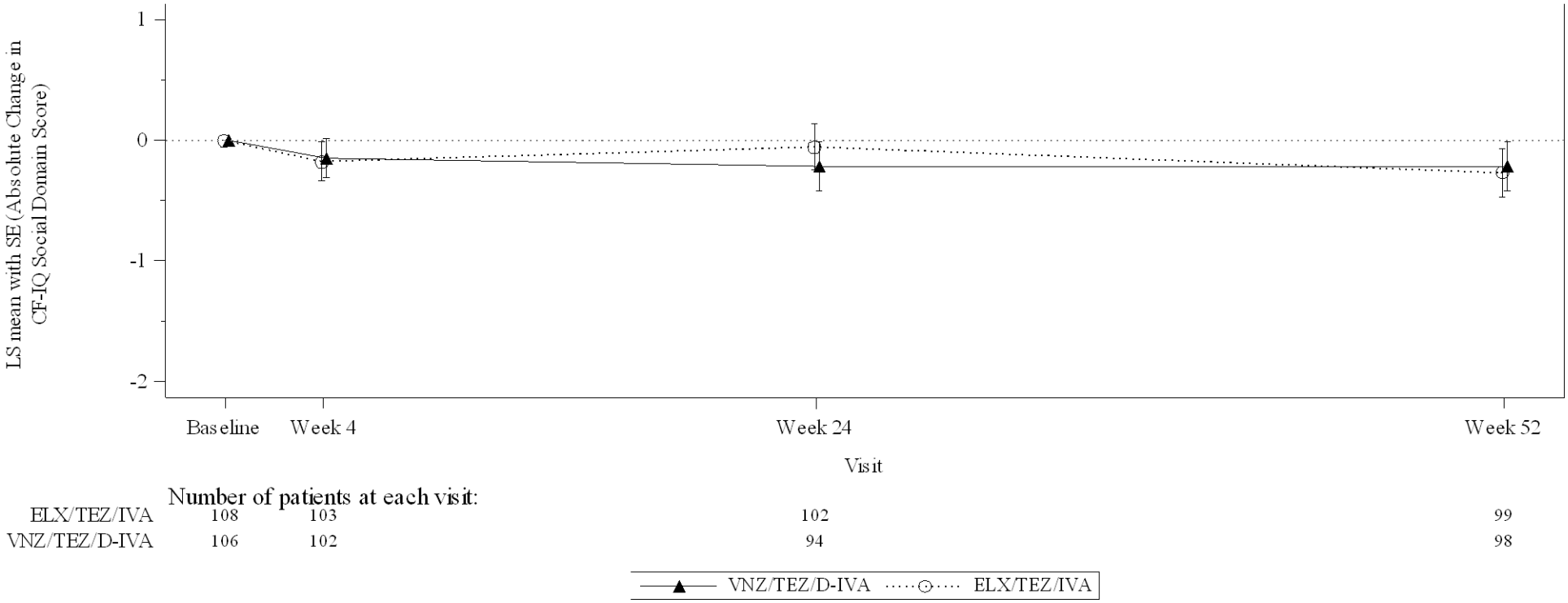
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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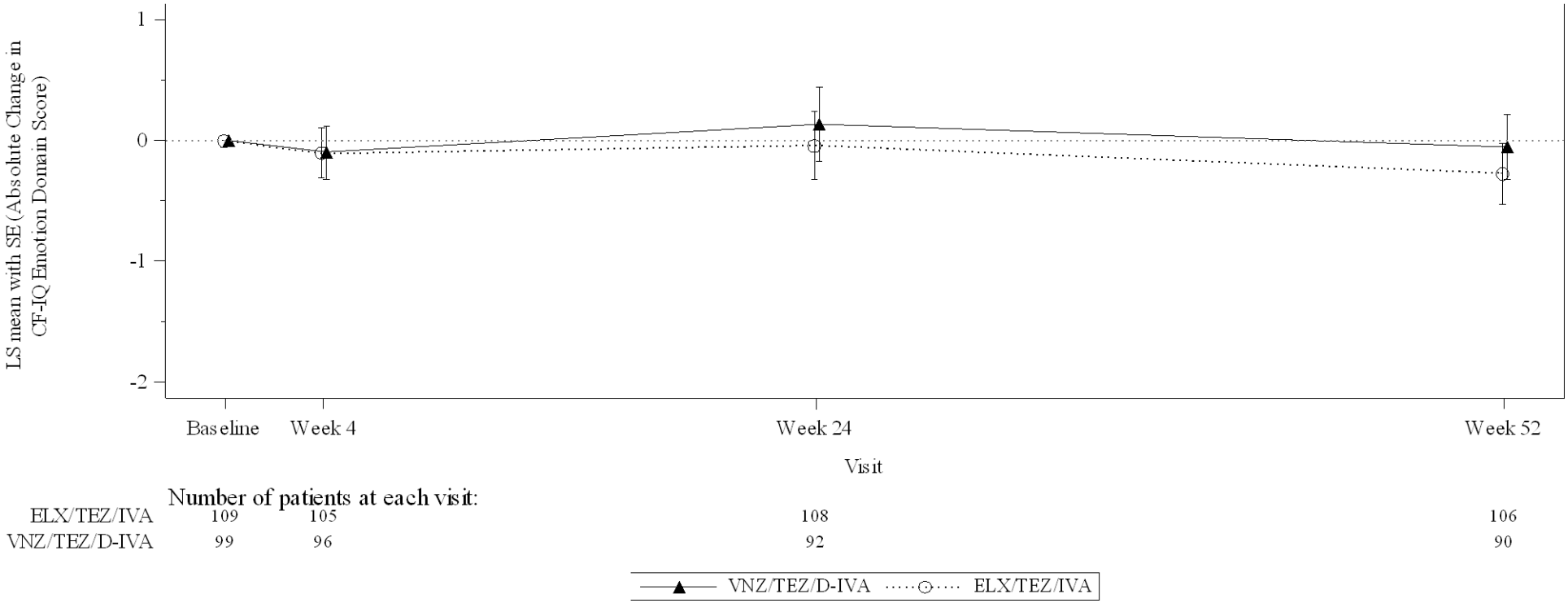
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
ppFEV$_1$ at baseline <70 %



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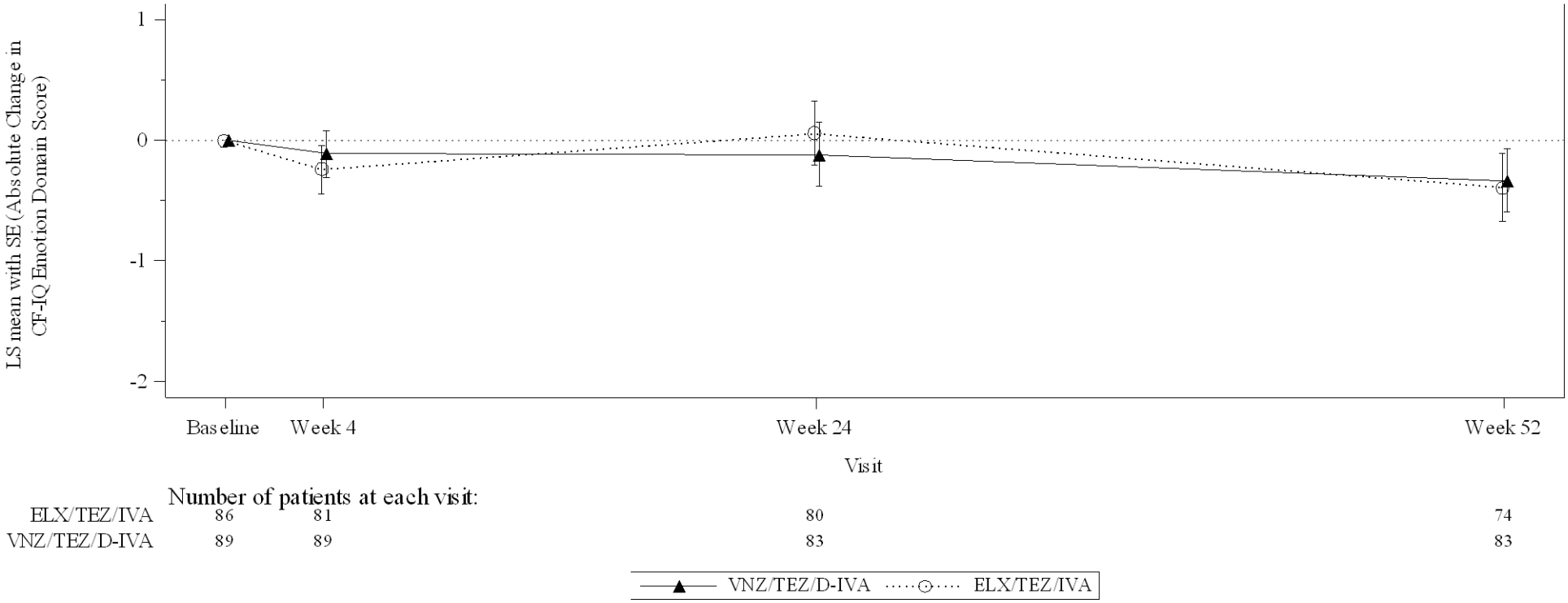
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
ppFEV$_1$ at baseline ≥70 %



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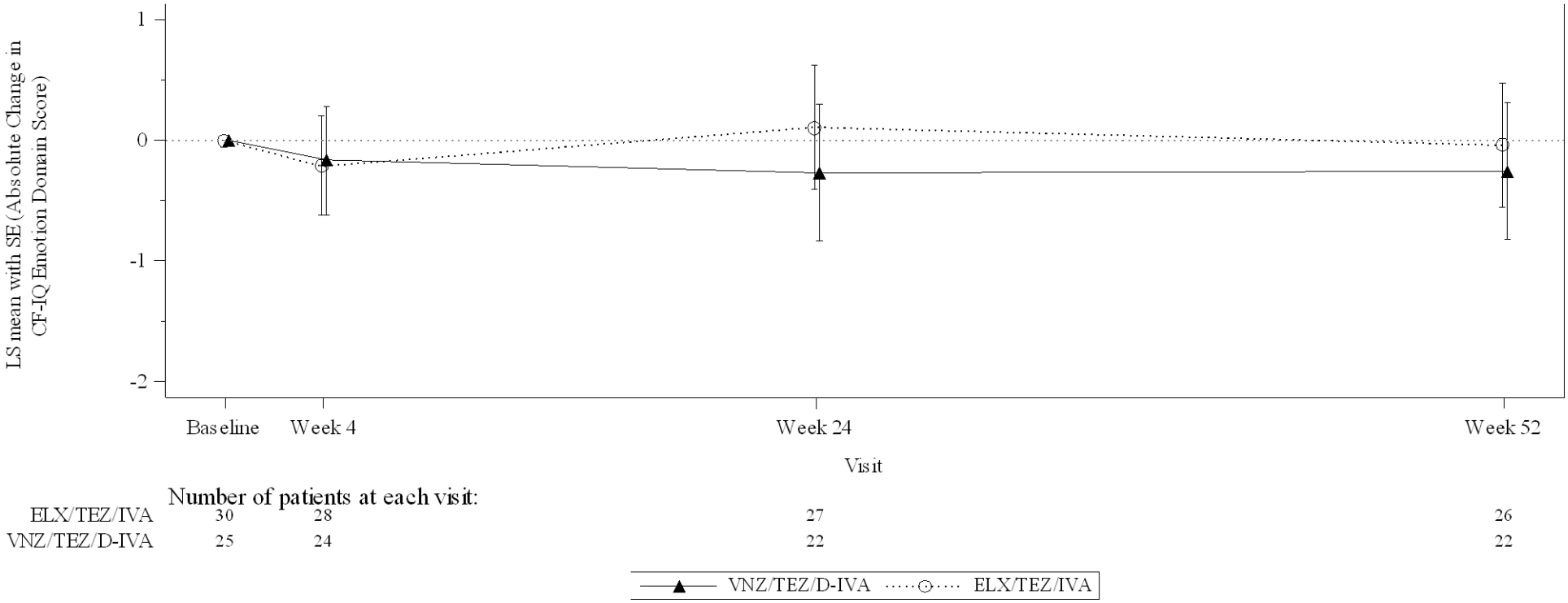
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
Age at screening <18 years



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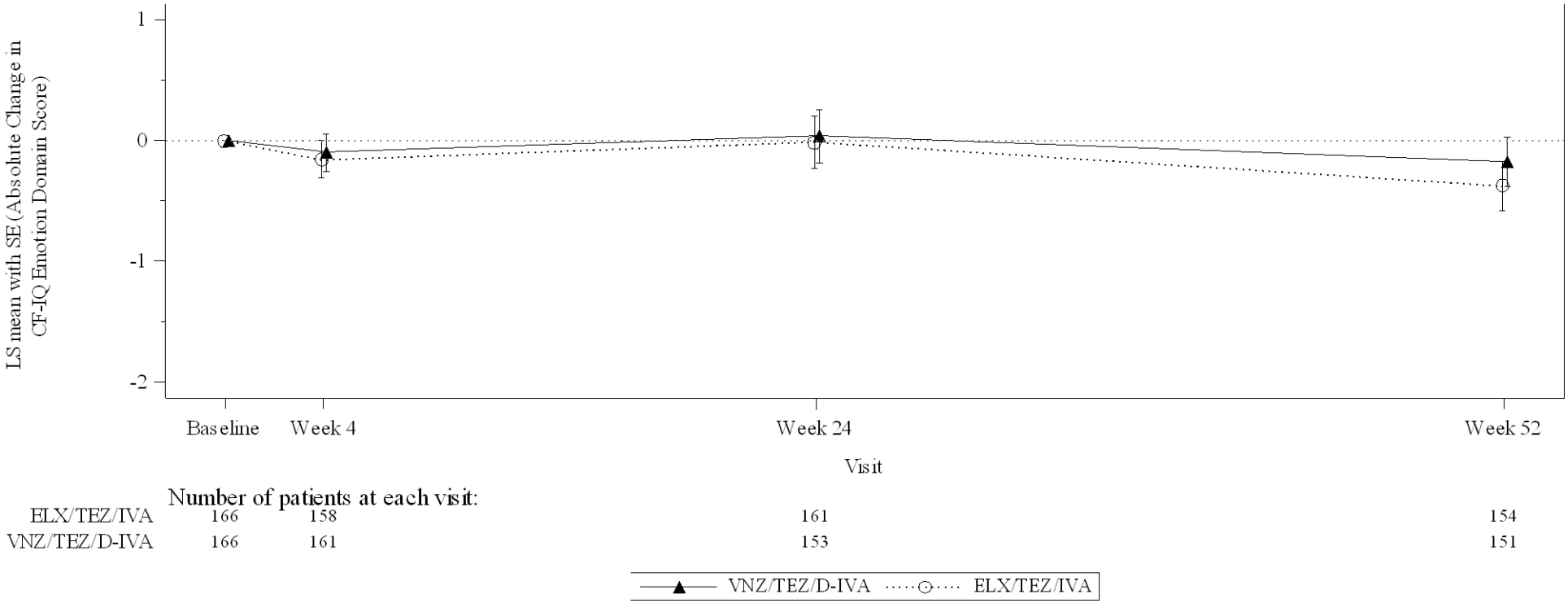
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
Age at screening ≥18 years



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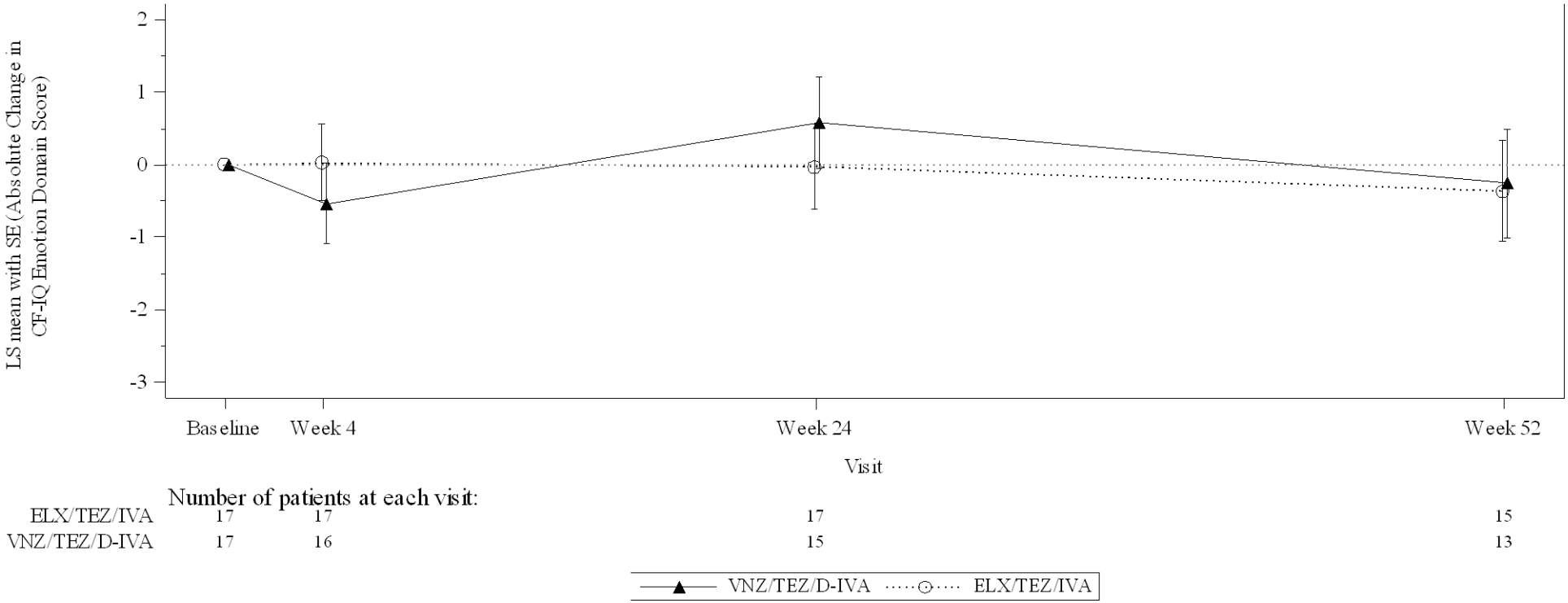
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
SwCl at baseline <30 mmol/L



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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
SwCl at baseline ≥30 mmol/L

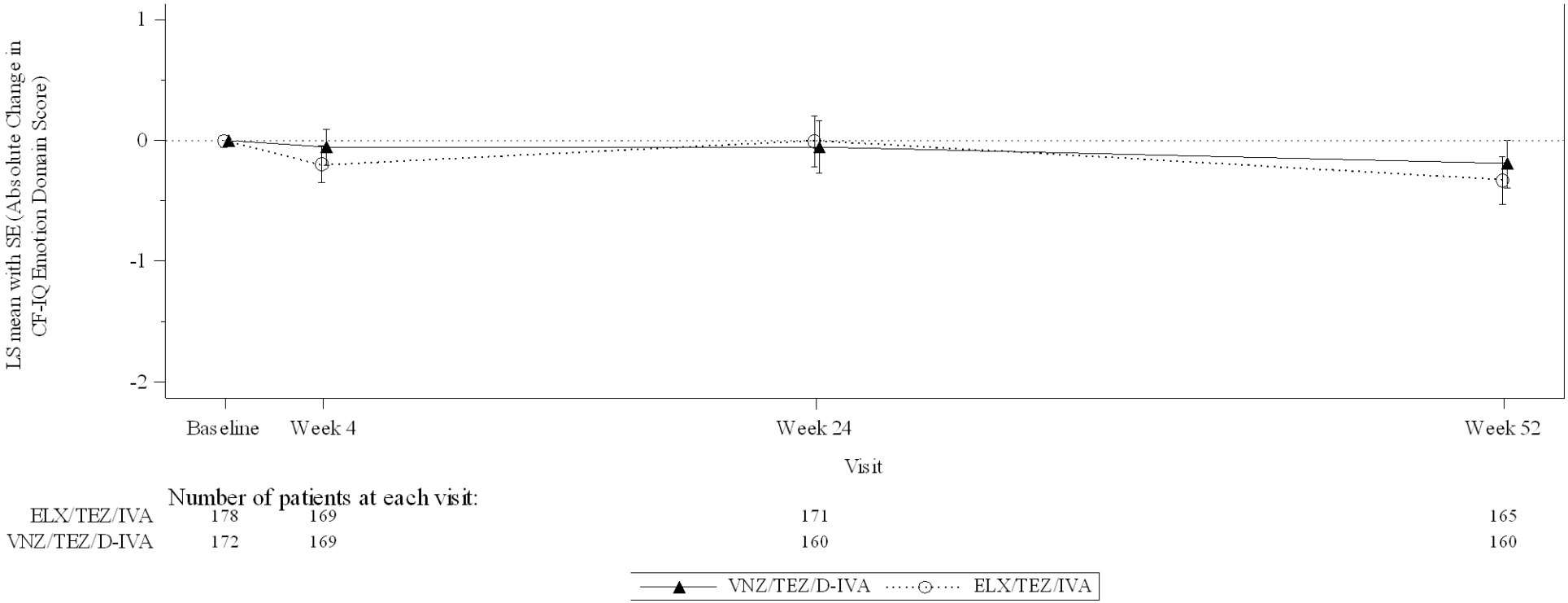

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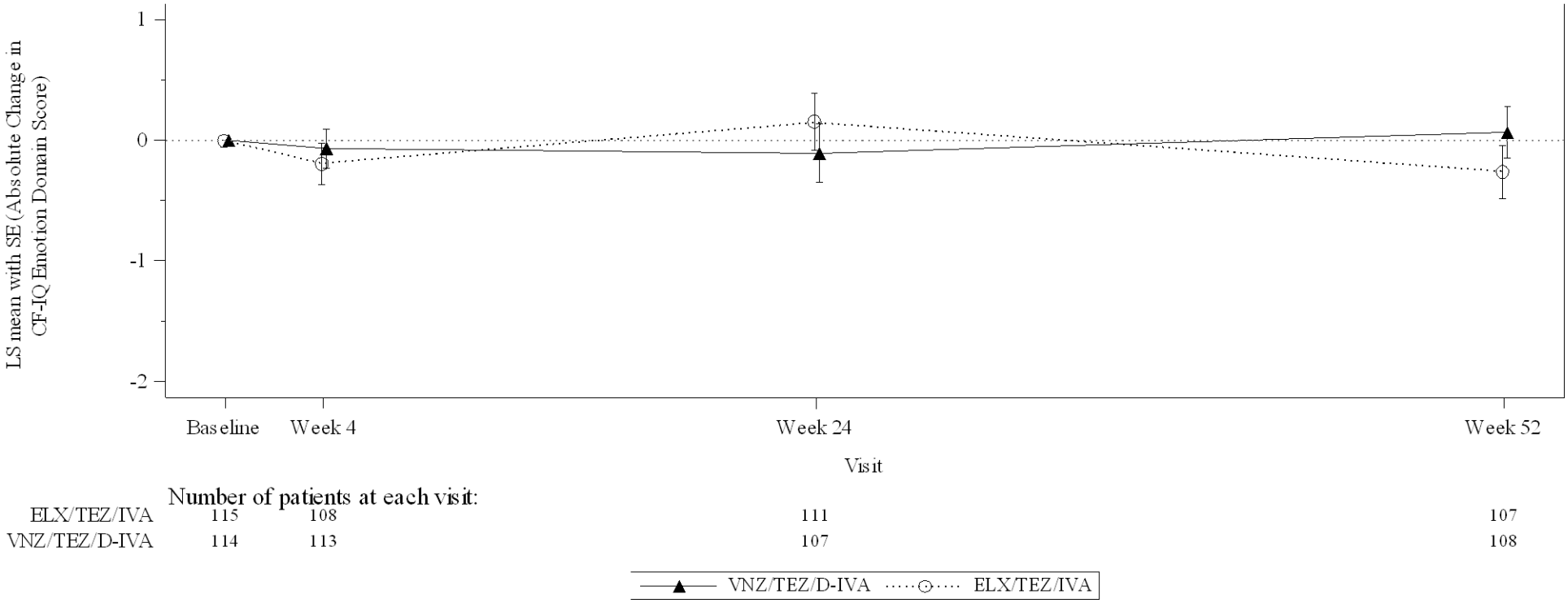
Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
Sex = Male



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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
Sex = Female

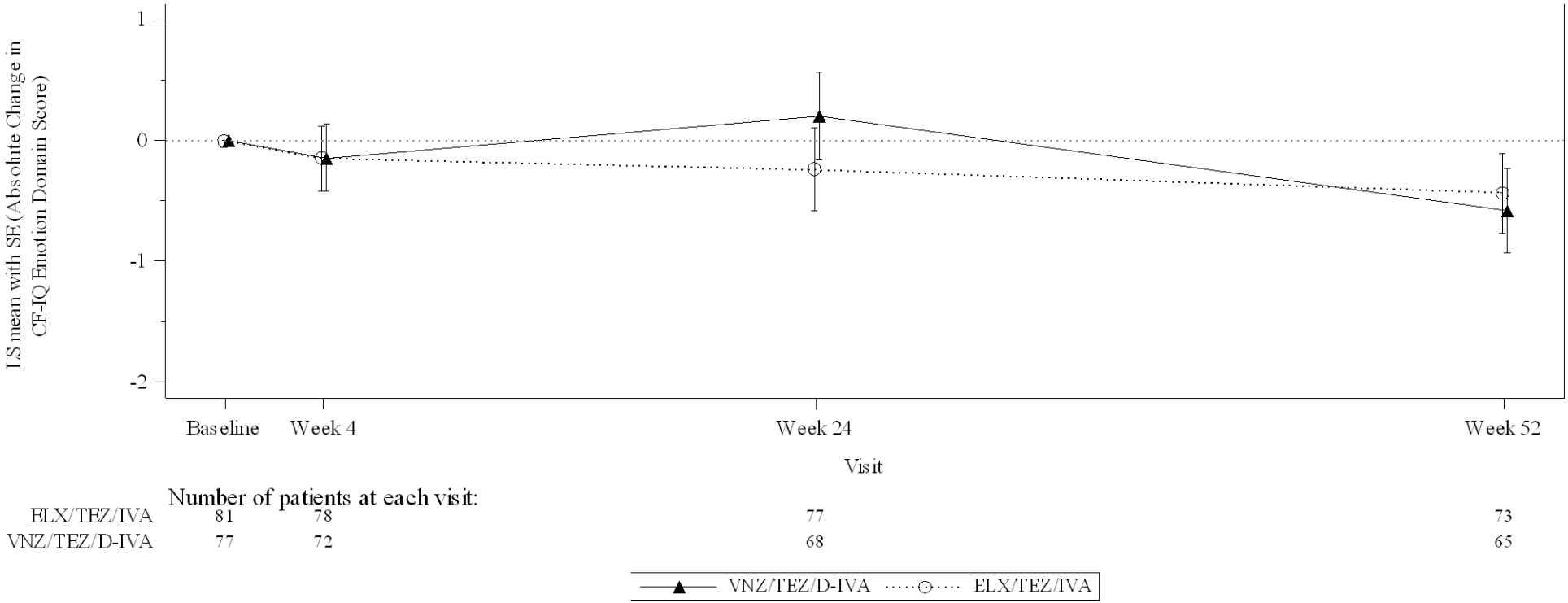

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Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
Region = North America

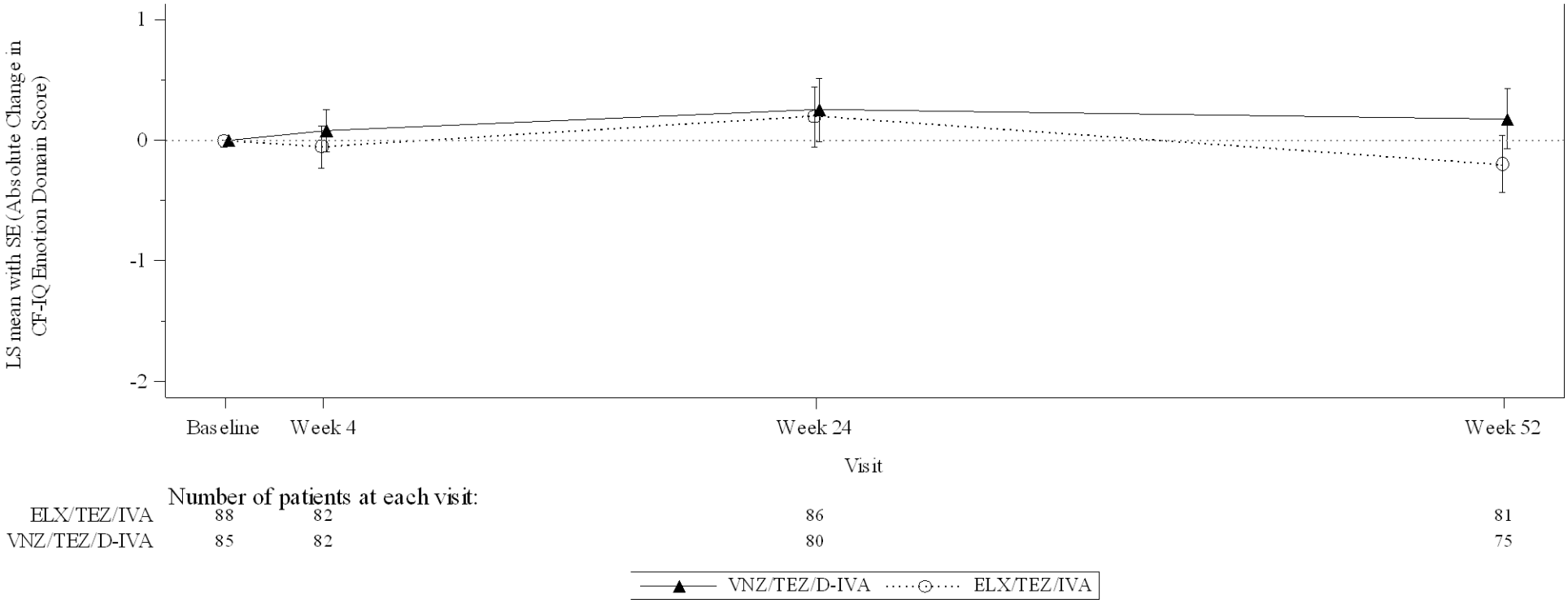

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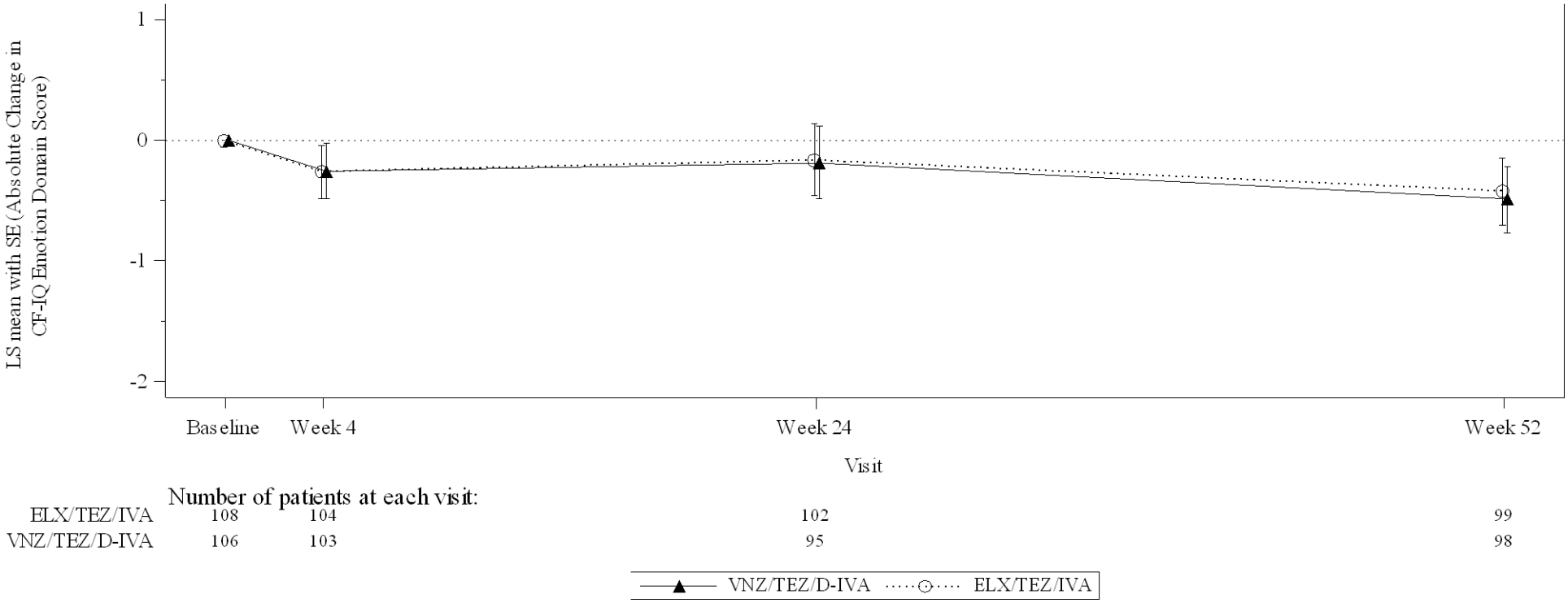
Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
Region = Rest of World



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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
ppFEV$_1$ at baseline <70 %

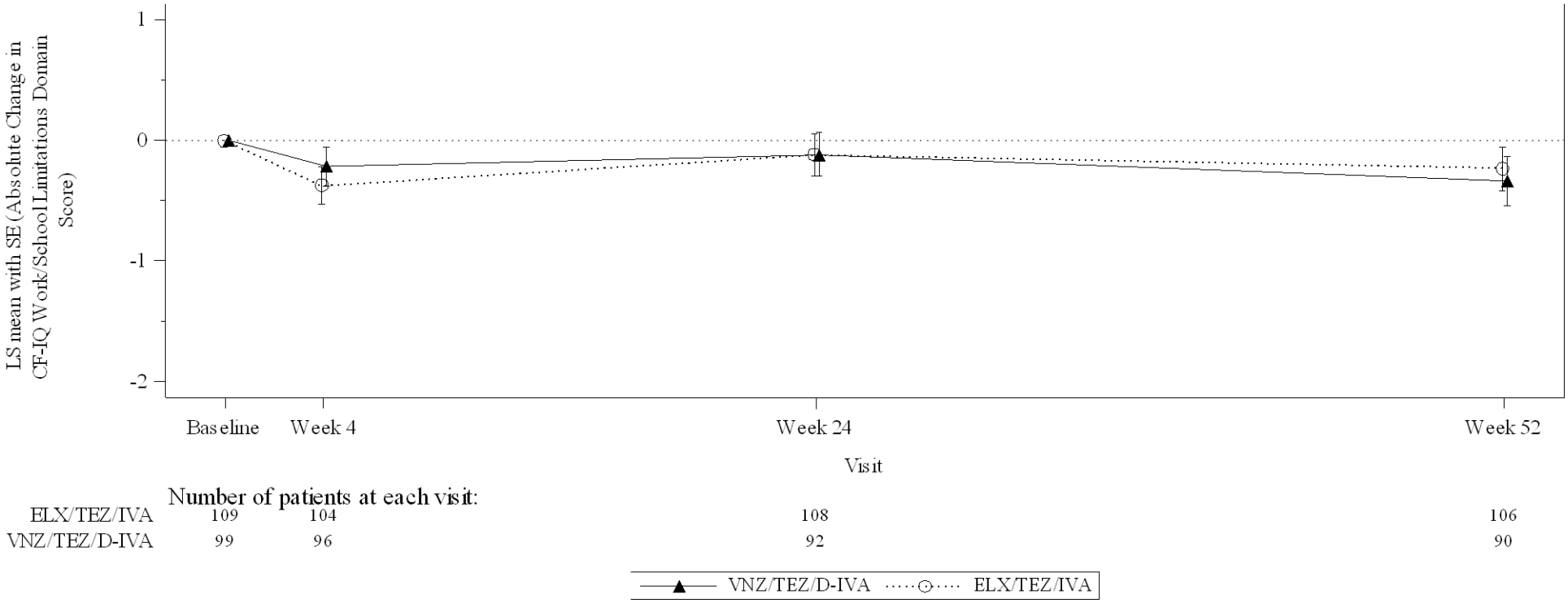

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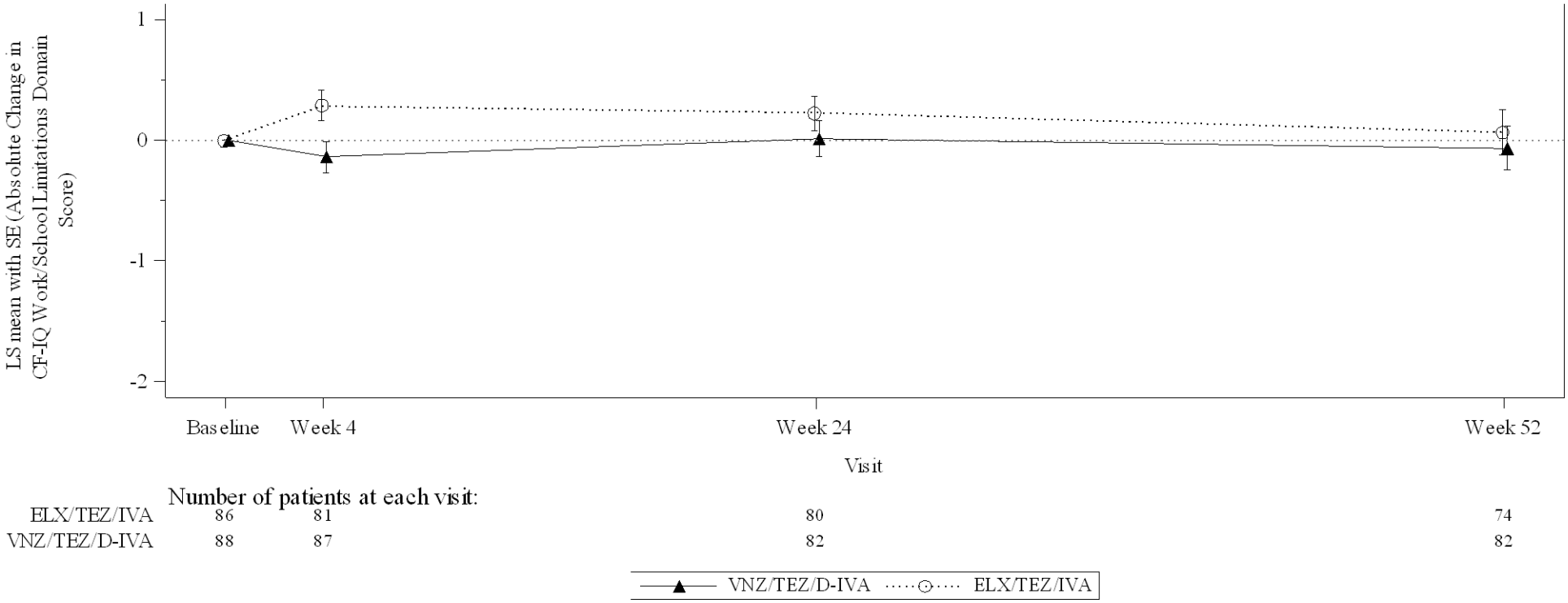
Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
ppFEV$_1$ at baseline ≥70 %



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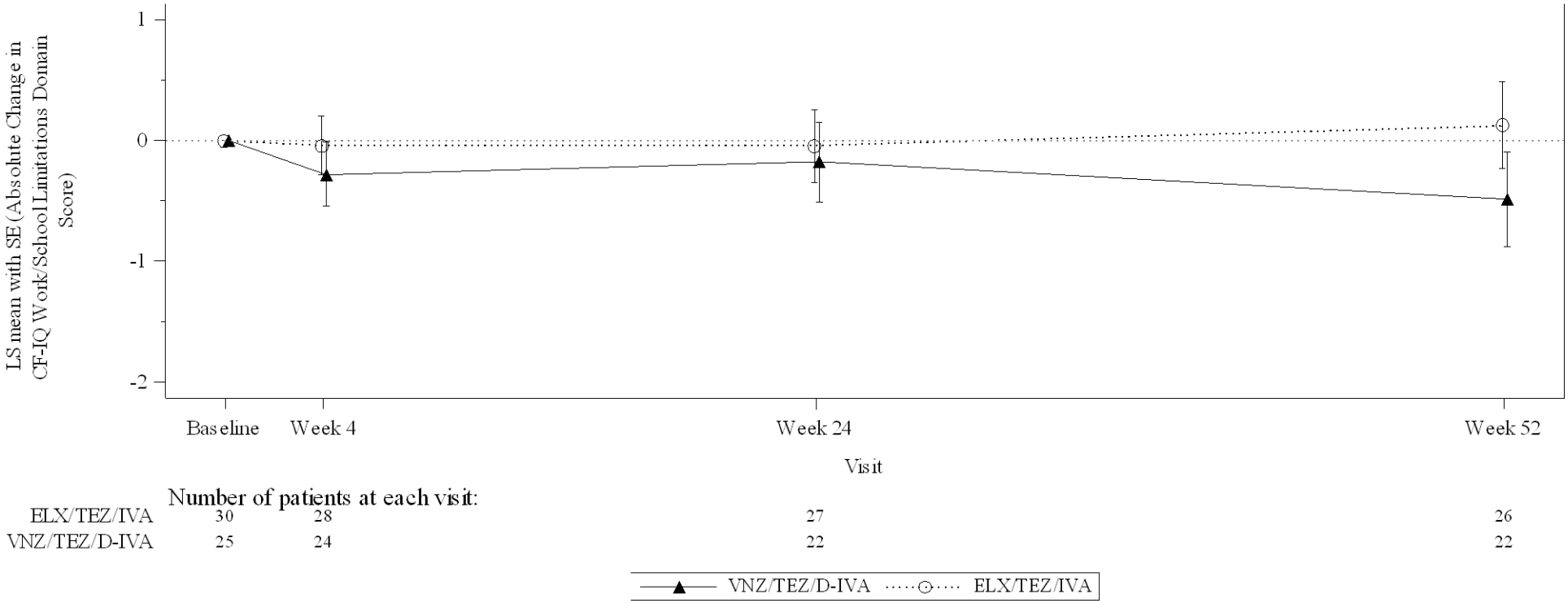
Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
Age at screening <18 years



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Program: GMA\VX121\germandossier\clinstat_prod\121-102\f-qs-abs-cfiq-52wks-sub-102.sas Creation: 17DEC2024 13:48

Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
Age at screening ≥18 years

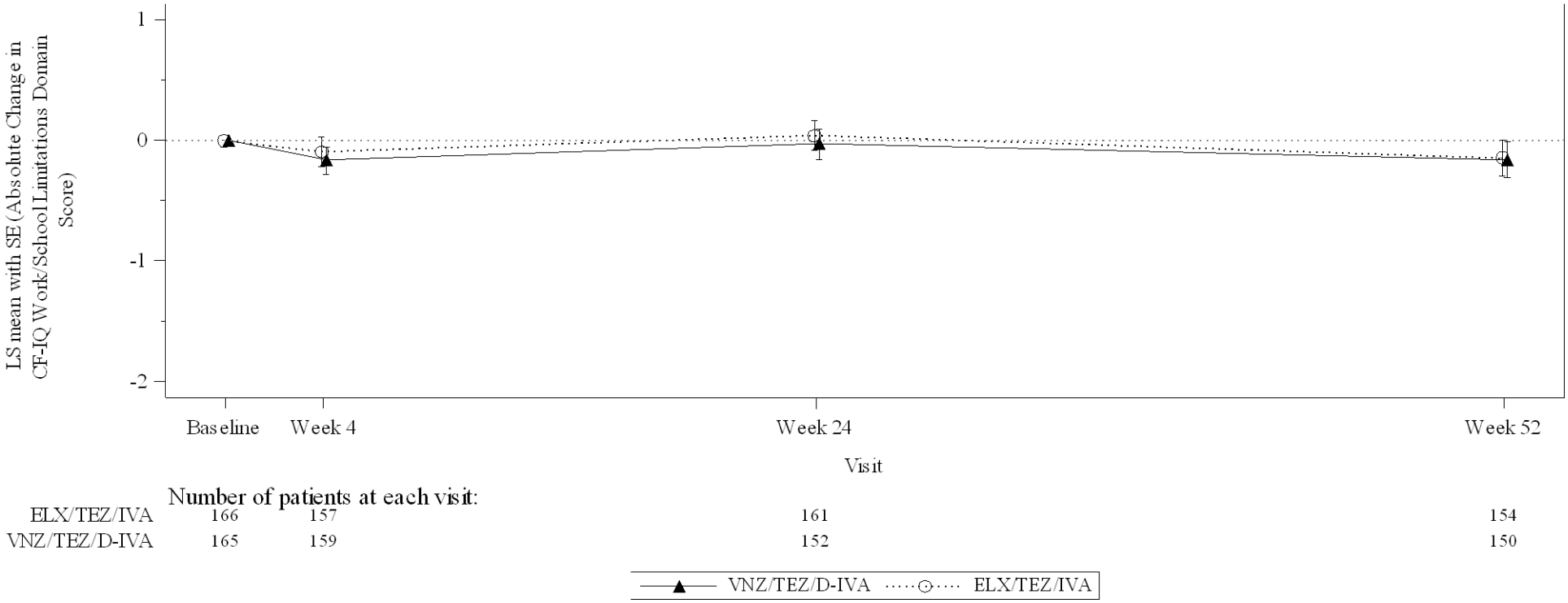

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Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
SwCl at baseline <30 mmol/L

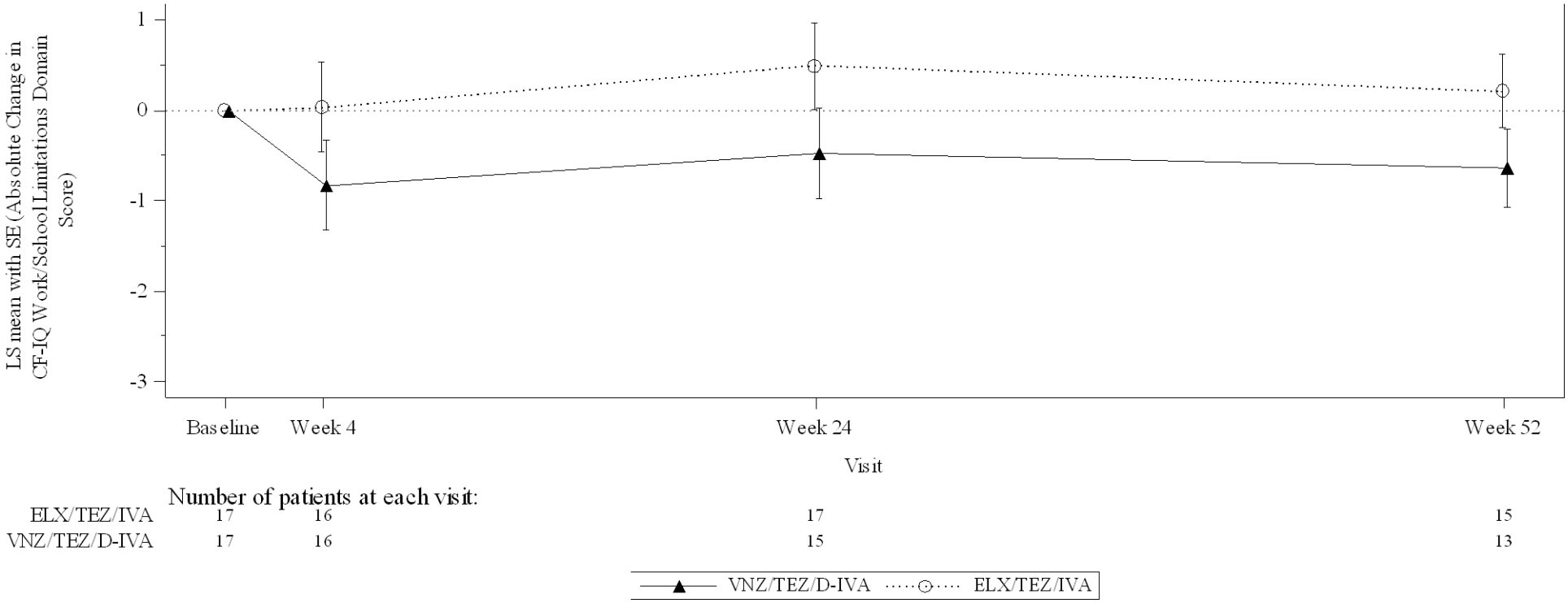

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Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
SwCl at baseline ≥30 mmol/L

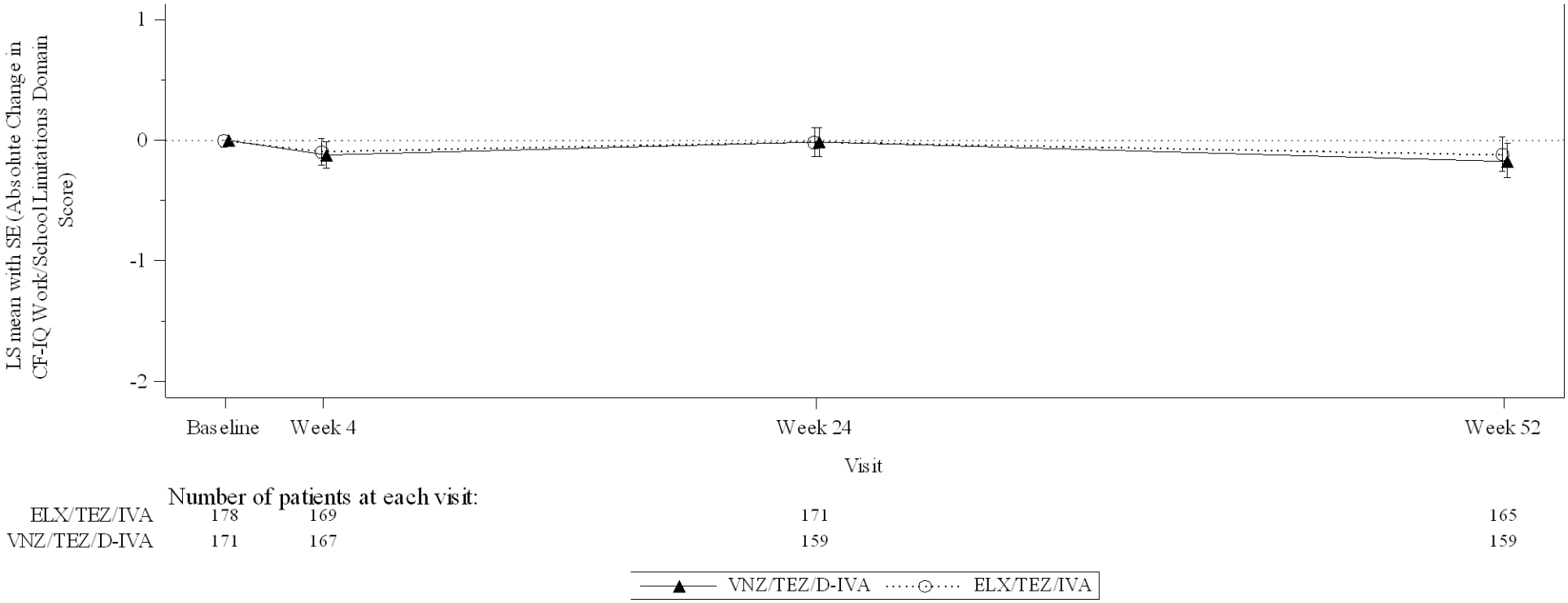

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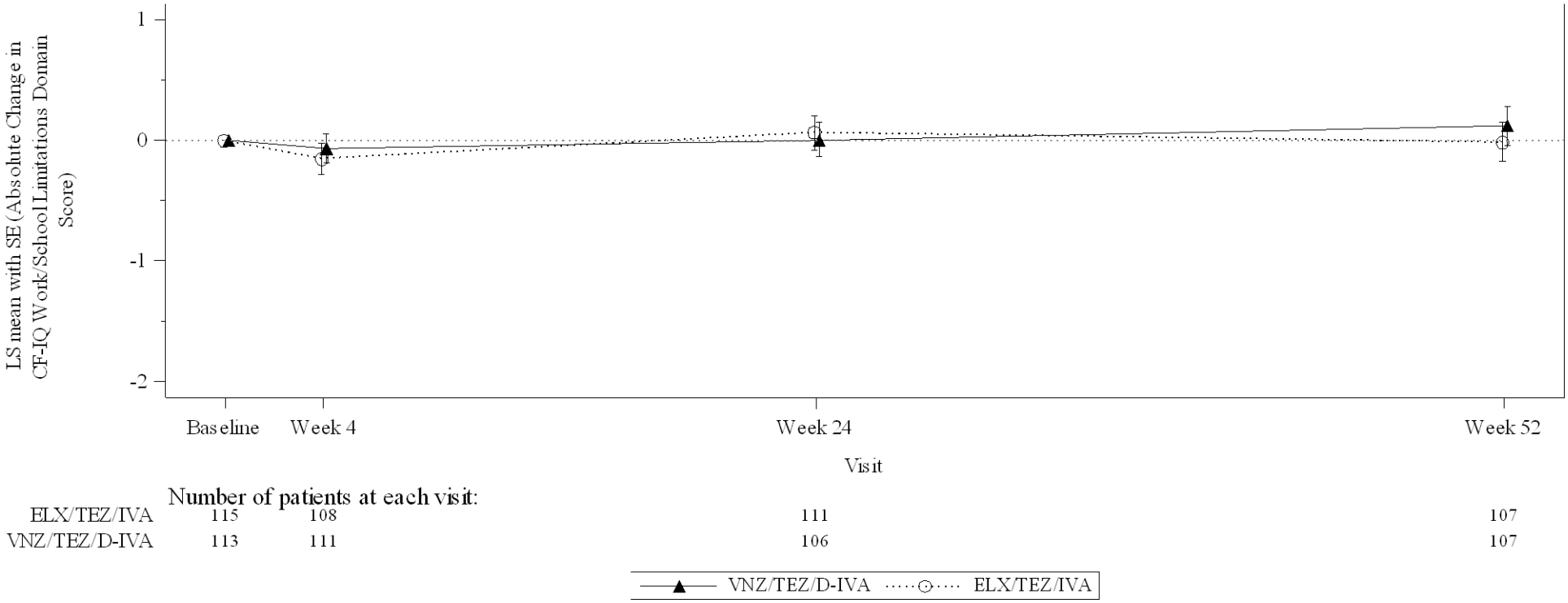
Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
Sex = Male



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- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

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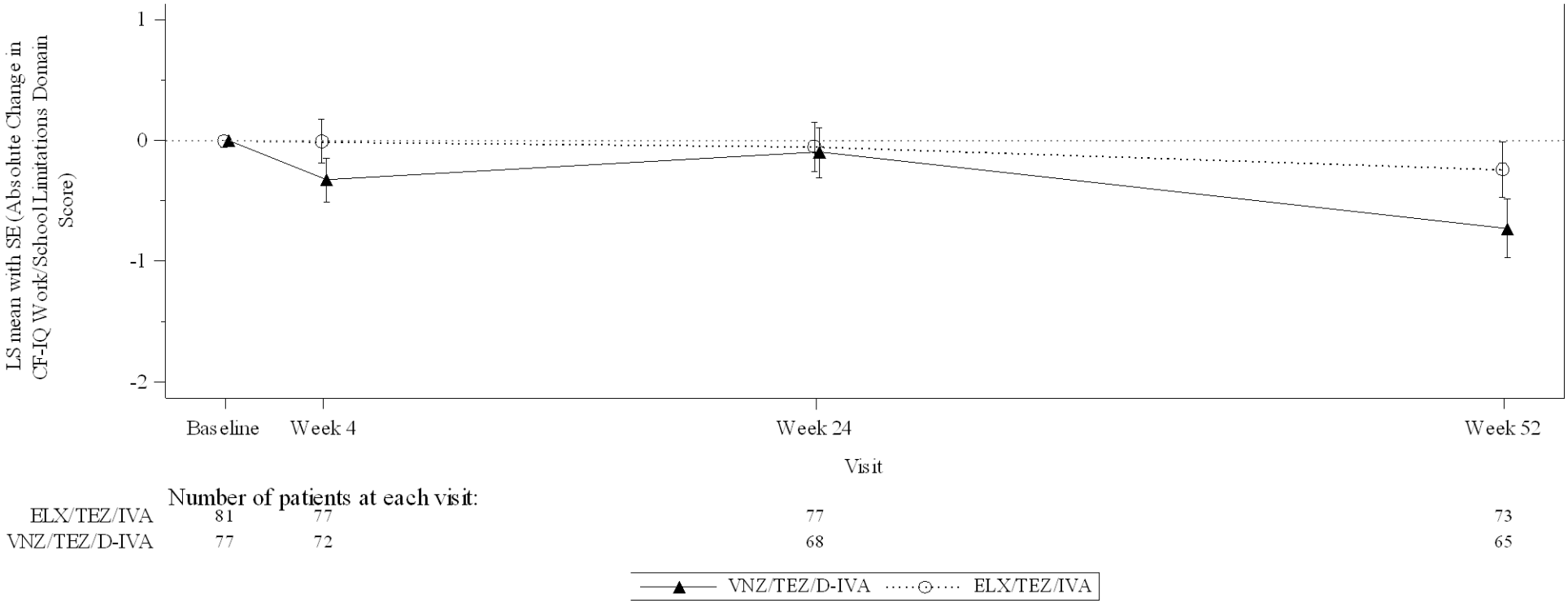
Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

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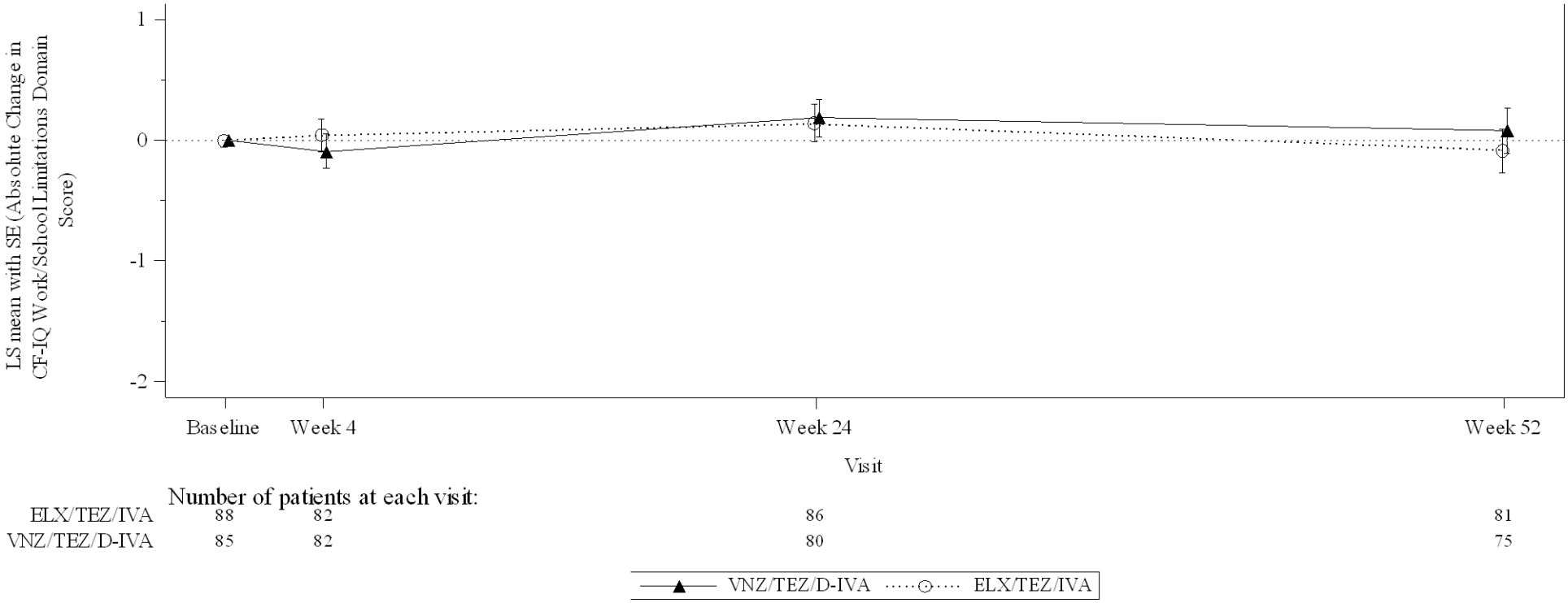
Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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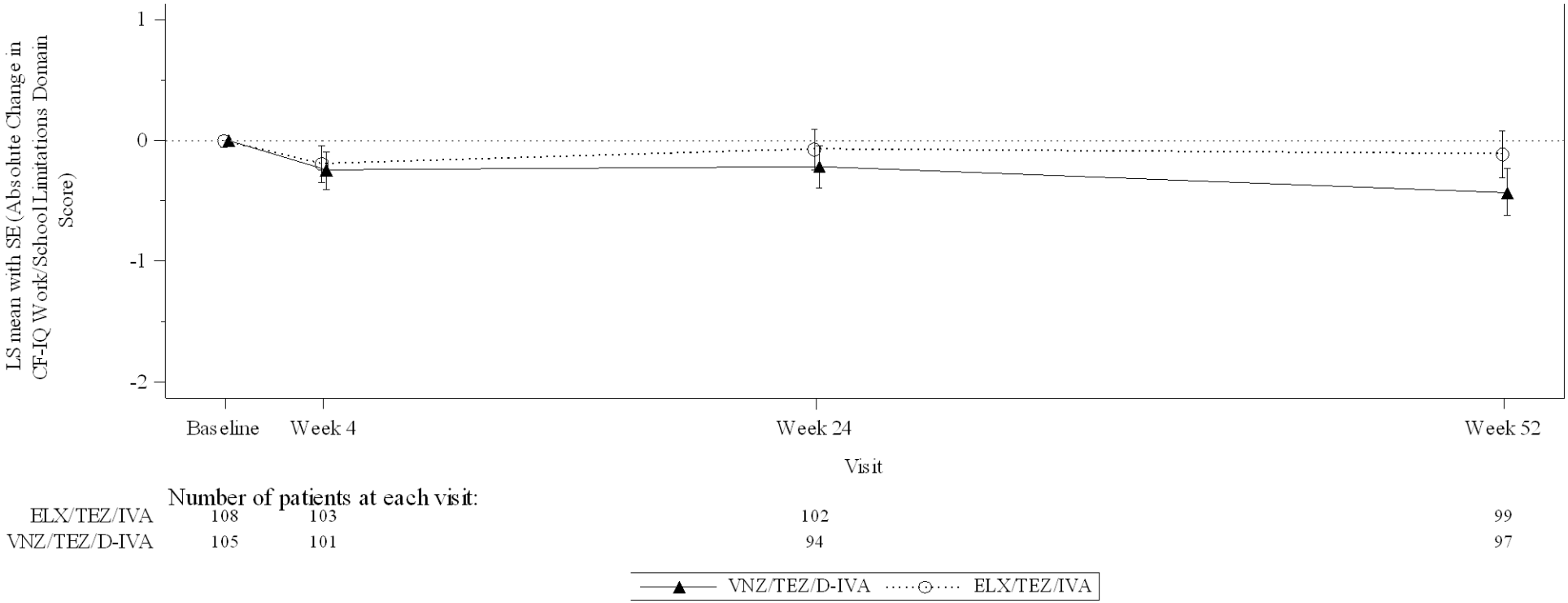
Figure 1.2.2.13.2
Study VX20-121-102: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

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Zusatzanalysen Studie VX20-121-103

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Table 2.1.1.1
Study VX20-121-103: Summary of Duration of Observation (Weeks) per Endpoint
Full Analysis Set

Duration of observation (weeks)	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Overall Study Observation Time		
n	289	284
Mean (SD)	51.26 (5.63)	50.42 (7.77)
Median	52.14	52.14
Min, Max	4.29, 56.86	4.57, 56.14
$ppFEV_1$ (percentage points)		
n	289	284
Mean (SD)	50.69 (6.46)	49.73 (8.84)
Median	52.14	52.14
Min, Max	4.29, 56.86	2.00, 56.14
BMI (kg/m^2)		
n	289	284
Mean (SD)	50.92 (6.17)	49.81 (8.69)
Median	52.14	52.14
Min, Max	4.29, 56.86	4.43, 56.00
BMI z-score		
n	42	53
Mean (SD)	48.21 (11.70)	45.76 (13.32)
Median	52.00	52.14
Min, Max	4.29, 56.86	4.43, 53.00
Sweat Chloride (mmol/L)		
n	286	283
Mean (SD)	50.54 (6.74)	48.62 (10.80)
Median	52.14	52.14
Min, Max	4.29, 53.71	0.14, 55.86

- Observation duration [weeks] is defined as (date of last observation - date of randomization +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results.

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Table 2.1.1.1
Study VX20-121-103: Summary of Duration of Observation (Weeks) per Endpoint
Full Analysis Set

Duration of observation (weeks)	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Weight (kg)		
n	289	284
Mean (SD)	51.20 (5.86)	50.19 (8.43)
Median	52.14	52.14
Min, Max	4.29, 56.86	4.43, 56.00
Pulmonary Exacerbation		
n	289	284
Mean (SD)	51.17 (5.59)	50.35 (7.75)
Median	52.14	52.14
Min, Max	4.29, 53.71	4.57, 53.86
CFQ-R		
n	289	284
Mean (SD)	50.80 (6.59)	49.88 (9.08)
Median	52.14	52.14
Min, Max	4.29, 53.71	0.14, 55.86
TSQM		
n	148	138
Mean (SD)	24.47 (25.58)	26.54 (25.45)
Median	0.71	26.43
Min, Max	0.00, 53.14	0.14, 53.86
CF-IQ		
n	288	284
Mean (SD)	50.39 (7.82)	48.70 (11.54)
Median	52.14	52.14
Min, Max	3.57, 53.71	0.14, 53.86

- Observation duration [weeks] is defined as (date of last observation - date of randomization +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results.

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Table 2.1.1.1
Study VX20-121-103: Summary of Duration of Observation (Weeks) per Endpoint
Full Analysis Set

Duration of observation (weeks)	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Safety		
n	289	284
Mean (SD)	50.72 (6.85)	49.70 (9.15)
Median	52.14	52.14
Min, Max	4.14, 56.71	4.57, 56.00

- Observation duration [weeks] is defined as (date of last observation - date of randomization +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results.

Table 2.1.2.1
Study VX20-121-103: Summary of Patients with Ongoing Antibiotic Medications at Baseline or at Week 52
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline, N1	289	284
Subjects with 0 ongoing AB	121 (41.87)	128 (45.07)
Subjects with 1 ongoing AB	104 (35.99)	88 (30.99)
Subjects with ≥ 2 ongoing AB	64 (22.15)	68 (23.94)
Subjects with ≥ 1 ongoing IV AB	1 (0.35)	1 (0.35)
Week 52, N1	278	264
Subjects with 0 ongoing AB	122 (43.88)	116 (43.94)
Subjects with 1 ongoing AB	94 (33.81)	95 (35.98)
Subjects with ≥ 2 ongoing AB	62 (22.30)	53 (20.08)
Subjects with ≥ 1 ongoing IV AB	5 (1.80)	2 (0.76)

- AB: Antibiotic medications are defined as those medications with the ATC level 2 names of "ANTIBACTERIALS FOR SYSTEMIC USE" and "ANTIMYCOBACTERIALS".
- Antibiotic medications included in this summary refer to those with route being "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- IV antibiotic medications refer to those with route being "INTRAVENOUS" or "INTRAVENOUS BOLUS".
- Ongoing antibiotic medications at baseline refer to those with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing antibiotic medications at Week 52 refer to those with start date < Week 52 visit date and the end date ≥ Week 52 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 52 visit, respectively. The percentages in this table are calculated based on N1.

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Table 2.1.2.2
Study VX20-121-103: Summary of Patients with Antibiotic Medications during the Study Treatment Period
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
All subjects	289	284
Subjects with 0 AB	32 (11.07)	37 (13.03)
Subjects with 1-3 AB	127 (43.94)	129 (45.42)
Subjects with ≥ 4 AB	130 (44.98)	118 (41.55)
Subjects with 0 IV AB	238 (82.35)	240 (84.51)
Subjects with 1 IV AB	9 (3.11)	11 (3.87)
Subjects with ≥ 2 IV AB	42 (14.53)	33 (11.62)
Subjects with 0 ongoing antibiotic medications at baseline	121	128
Subjects with 0 AB	32 (26.45)	37 (28.91)
Subjects with 1-3 AB	60 (49.59)	65 (50.78)
Subjects with ≥ 4 AB	29 (23.97)	26 (20.31)
Subjects with 0 IV AB	105 (86.78)	114 (89.06)
Subjects with 1 IV AB	4 (3.31)	4 (3.13)
Subjects with ≥ 2 IV AB	12 (9.92)	10 (7.81)

- AB: Antibiotic medications are defined as those medications with the ATC level 2 names of "ANTIBACTERIALS FOR SYSTEMIC USE" and "ANTIMYCOBACTERIALS".
- Antibiotic medications included in this summary refer to those with route being "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- IV antibiotic medications refer to those with route being "INTRAVENOUS" or "INTRAVENOUS BOLUS".
- Antibiotic medications during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period, and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 2.1.3.1
Study VX20-121-103: Summary of Patients with Ongoing Physiotherapies at Baseline or at Week 52
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline, N1	289	284
Subjects with 0 ongoing PT	155 (53.63)	162 (57.04)
Subjects with 1 ongoing PT	121 (41.87)	104 (36.62)
Subjects with ≥ 2 ongoing PT	13 (4.50)	18 (6.34)
Week 52, N1	278	264
Subjects with 0 ongoing PT	148 (53.24)	150 (56.82)
Subjects with 1 ongoing PT	117 (42.09)	96 (36.36)
Subjects with ≥ 2 ongoing PT	13 (4.68)	18 (6.82)

- PT: Physiotherapies refer to the non-pharmacological treatments with preferred names of "Positive expiratory pressure therapy", "Airway secretion clearance therapy", "Positive end-expiratory pressure", or "Physiotherapy chest".
- The ongoing physiotherapy at baseline is defined as a physiotherapy whose start date is prior to first dose date of study drug in the Treatment Period and the end date is ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing physiotherapy at Week 52 is defined as a physiotherapy whose start date is prior to Week 52 visit date and the end date is ≥ Week 52 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 52 visit, respectively. The percentages in this table are calculated based on N1.

Table 2.1.3.2
Study VX20-121-103: Summary of Patients with Physiotherapies during the Study Treatment Period
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
All subjects	289	284
Subjects with 0 PT	154 (53.29)	160 (56.34)
Subjects with 1 PT	120 (41.52)	104 (36.62)
Subjects with ≥ 2 PT	15 (5.19)	20 (7.04)
Subjects with 0 ongoing physiotherapies at baseline	155	162
Subjects with 0 PT	154 (99.35)	160 (98.77)
Subjects with 1 PT	1 (0.65)	1 (0.62)
Subjects with ≥ 2 PT	0	1 (0.62)

- PT: Physiotherapies refer to the non-pharmacological treatments with preferred names of "Positive expiratory pressure therapy", "Airway secretion clearance therapy", "Positive end-expiratory pressure", or "Physiotherapy chest".
- Physiotherapies during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

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Table 2.1.4.1
Study VX20-121-103: Summary of Patients with Ongoing Inhaled Medications at Baseline or at Week 52
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline, N1	289	284
Subjects with 0 ongoing IM	25 (8.65)	15 (5.28)
Subjects with 1 ongoing IM	30 (10.38)	40 (14.08)
Subjects with ≥ 2 ongoing IM	234 (80.97)	229 (80.63)
Week 52, N1	278	264
Subjects with 0 ongoing IM	24 (8.63)	11 (4.17)
Subjects with 1 ongoing IM	31 (11.15)	39 (14.77)
Subjects with ≥ 2 ongoing IM	223 (80.22)	214 (81.06)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB) and for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 52 refer to those IMs with start date < Week 52 visit date and the end date ≥ Week 52 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 52 visit, respectively. The percentages in this table are calculated based on N1.

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Table 2.1.4.2
Study VX20-121-103: Summary of Patients with Inhaled Medications during the Study Treatment Period
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
All subjects	289	284
Subjects with 0 IM	21 (7.27)	10 (3.52)
Subjects with 1 IM	27 (9.34)	35 (12.32)
Subjects with ≥ 2 IM	241 (83.39)	239 (84.15)
Subjects with 0 ongoing inhaled medications at baseline	25	15
Subjects with 0 IM	21 (84.00)	10 (66.67)
Subjects with 1 IM	2 (8.00)	2 (13.33)
Subjects with ≥ 2 IM	2 (8.00)	3 (20.00)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB) and for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

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Table 2.1.4.3
Study VX20-121-103: Summary of Patients with Ongoing Inhaled Medications for Mucolytics at Baseline or at Week 52
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline, N1	289	284
Subjects with 0 ongoing IM	59 (20.42)	71 (25.00)
Subjects with 1 ongoing IM	107 (37.02)	102 (35.92)
Subjects with ≥ 2 ongoing IM	123 (42.56)	111 (39.08)
Week 52, N1	278	264
Subjects with 0 ongoing IM	64 (23.02)	70 (26.52)
Subjects with 1 ongoing IM	102 (36.69)	93 (35.23)
Subjects with ≥ 2 ongoing IM	112 (40.29)	101 (38.26)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 52 refer to those IMs with start date < Week 52 visit date and the end date ≥ Week 52 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 52 visit, respectively. The percentages in this table are calculated based on N1.

Table 2.1.4.4
Study VX20-121-103: Summary of Patients with Inhaled Medications for Mucolytics during the Study Treatment Period
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
All subjects	289	284
Subjects with 0 IM	54 (18.69)	64 (22.54)
Subjects with 1 IM	103 (35.64)	102 (35.92)
Subjects with ≥ 2 IM	132 (45.67)	118 (41.55)
Subjects with 0 ongoing inhaled medications at baseline	59	71
Subjects with 0 IM	54 (91.53)	64 (90.14)
Subjects with 1 IM	5 (8.47)	3 (4.23)
Subjects with ≥ 2 IM	0	4 (5.63)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 2.1.4.5
Study VX20-121-103: Summary of Patients with Ongoing Inhaled Medications for Obstructive Airway Disease at Baseline or at Week 52
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline, N1	289	284
Subjects with 0 ongoing IM	48 (16.61)	30 (10.56)
Subjects with 1 ongoing IM	88 (30.45)	109 (38.38)
Subjects with ≥ 2 ongoing IM	153 (52.94)	145 (51.06)
Week 52, N1	278	264
Subjects with 0 ongoing IM	45 (16.19)	23 (8.71)
Subjects with 1 ongoing IM	89 (32.01)	102 (38.64)
Subjects with ≥ 2 ongoing IM	144 (51.80)	139 (52.65)

- IM: Inhaled medications refer to those medications for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 52 refer to those IMs with start date < Week 52 visit date and the end date ≥ Week 52 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 52 visit, respectively. The percentages in this table are calculated based on N1.

Table 2.1.4.6
Study VX20-121-103: Summary of Patients with Inhaled Medications for Obstructive Airway Disease during the Study Treatment Period
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
All subjects	289	284
Subjects with 0 IM	42 (14.53)	23 (8.10)
Subjects with 1 IM	84 (29.07)	101 (35.56)
Subjects with ≥ 2 IM	163 (56.40)	160 (56.34)
Subjects with 0 ongoing inhaled medications at baseline	48	30
Subjects with 0 IM	42 (87.50)	23 (76.67)
Subjects with 1 IM	4 (8.33)	2 (6.67)
Subjects with ≥ 2 IM	2 (4.17)	5 (16.67)

- IM: Inhaled medications refer to those medications for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 2.1.5.1
Study VX20-121-103: Summary of Patients with Ongoing CF-related Medications at Baseline or at Week 52
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline, N1	289	284
Subjects with 0 ongoing CF-related medications	2 (0.69)	3 (1.06)
Subjects with 1 ongoing CF-related medications	8 (2.77)	6 (2.11)
Subjects with 2 ongoing CF-related medications	18 (6.23)	14 (4.93)
Subjects with 3 ongoing CF-related medications	19 (6.57)	23 (8.10)
Subjects with 4 ongoing CF-related medications	37 (12.80)	36 (12.68)
Subjects with ≥5 ongoing CF-related medications	205 (70.93)	202 (71.13)
Week 52, N1	278	264
Subjects with 0 ongoing CF-related medications	2 (0.72)	3 (1.14)
Subjects with 1 ongoing CF-related medications	8 (2.88)	5 (1.89)
Subjects with 2 ongoing CF-related medications	16 (5.76)	8 (3.03)
Subjects with 3 ongoing CF-related medications	19 (6.83)	29 (10.98)
Subjects with 4 ongoing CF-related medications	36 (12.95)	31 (11.74)
Subjects with ≥5 ongoing CF-related medications	197 (70.86)	188 (71.21)

- CF-related medications: CF co-medications are defined as those medications with
o ATC level 2 names of "DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES", "DIGESTIVES, INCL. ENZYMES", "ANTIBACTERIALS FOR SYSTEMIC USE", "DRUGS USED IN DIABETES", "BILE AND LIVER THERAPY", "GENERAL NUTRIENTS";
o or ATC level 3 names of "DRUGS FOR CONSTIPATION", "PROPULSIVES";
o or ATC level 4 names of "MUCOLYTICS".
In addition, the route of administration for "DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES" and "MUCOLYTICS" requires to be "RESPIRATORY (INHALATION)" and the route for "ANTIBACTERIALS FOR SYSTEMIC USE" requires to be "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- The ongoing CF-related medications at baseline refer to those CF-related medications with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing CF-related medications at Week 52 refer to those CF-related medications with start date < Week 52 visit date and the end date ≥ Week 52 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 52 visit, respectively. The percentages in this table are calculated based on N1.

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Table 2.2.1.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	286	279
Mean (SD)	66.42 (14.85)	67.24 (14.63)
Week 52		
n	271	257
Mean (SD)	66.38 (15.28)	66.82 (14.85)
Absolute Change at Week 52		
n	269	254
Mean (SD)	-0.08 (5.39)	0.14 (4.87)
Absolute Change through Week 52 (MMRM)		
n	277	271
LS mean (SE)	-0.01 (0.24)	0.31 (0.24)
95% CI of LS mean	(-0.48, 0.47)	(-0.17, 0.79)
P-value within Treatment	0.9806	0.2061

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.31 (-0.36, 0.99)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3597
Hedges' G (SE)		0.08 (0.09)
Hedges' 95% CI		(-0.09, 0.25)
Hedges' P-value		0.3597

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	289	280
Mean (SD)	22.92 (3.27)	23.27 (4.02)
Week 52		
n	275	258
Mean (SD)	23.27 (3.45)	23.72 (4.15)
Absolute Change at Week 52		
n	275	254
Mean (SD)	0.27 (1.19)	0.37 (1.27)
Absolute Change at Week 52 (MMRM)		
n	266	248
LS mean (SE)	0.22 (0.07)	0.37 (0.08)
95% CI of LS mean	(0.07, 0.36)	(0.22, 0.52)
P-value within Treatment	0.0035	<0.0001
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-0.05, 0.36)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1442
Hedges' G (SE)		0.13 (0.09)
Hedges' 95% CI		(-0.04, 0.30)
Hedges' P-value		0.1447

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 for Subjects ≤20 Years at Baseline
Full Analysis Set

	ELX/TEZ/IVA N = 42	VNZ/TEZ/D-IVA N = 53
Baseline		
n	42	53
Mean (SD)	-0.30 (0.98)	-0.17 (0.95)
Week 52		
n	37	42
Mean (SD)	-0.35 (1.01)	0.02 (0.96)
Absolute Change at Week 52		
n	37	42
Mean (SD)	-0.08 (0.48)	0.15 (0.37)
Absolute Change at Week 52 (MMRM)		
n	35	42
LS mean (SE)	-0.13 (0.07)	0.11 (0.06)
95% CI of LS mean	(-0.27, 0.01)	(-0.01, 0.23)
P-value within Treatment	0.0643	0.0729
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.24 (0.06, 0.42)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0109
Hedges' G (SE)		0.59 (0.23)
Hedges' 95% CI		(0.13, 1.05)

- N is the number of subjects in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52
for Subjects ≤20 Years at Baseline
Full Analysis Set

	ELX/TEZ/IVA N = 42	VNZ/TEZ/D-IVA N = 53
Hedges' P-value		0.0125

- N is the number of subjects in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.4.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	282	282
Mean (SD)	42.07 (17.88)	43.43 (18.54)
Week 52		
n	269	254
Mean (SD)	40.06 (20.41)	38.16 (20.58)
Absolute Change at Week 52		
n	266	253
Mean (SD)	-2.38 (14.81)	-5.10 (14.03)
Absolute Change through Week 52 (MMRM)		
n	277	271
LS mean (SE)	-2.21 (0.64)	-4.98 (0.65)
95% CI of LS mean	(-3.46, -0.96)	(-6.25, -3.71)
P-value within Treatment	0.0006	<0.0001

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.4.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.77 (-4.55, -0.98)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0024
Hedges' G (SE)		-0.26 (0.09)
Hedges' 95% CI		(-0.43, -0.09)
Hedges' P-value		0.0025

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.4.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Non-missing value at Week 52, N1	269	254
Number of subjects with missing value at Week 52	20	30
SwCl <60 mmol/L at Week 52, n (%)	234 (80.97)	223 (78.52)
Relative Risk (RR) (95% CI)		0.9685 (0.8964, 1.0465)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4182*

- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- N/C: model does not converge.

Table 2.2.1.4.3
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Non-missing value at Week 52, N1	269	254
Number of subjects with missing value at Week 52	20	30
SwCl <30 mmol/L at Week 52, n (%)	93 (32.18)	100 (35.21)
Relative Risk (RR) (95% CI)		1.1124 (0.9223, 1.3416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2654*

- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- N/C: model does not converge.

Table 2.2.1.5
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	289	280
Mean (SD)	65.05 (13.35)	66.58 (13.98)
Week 52		
n	275	258
Mean (SD)	66.40 (13.22)	68.15 (14.01)
Absolute Change at Week 52		
n	275	254
Mean (SD)	0.97 (3.52)	1.33 (3.91)
Absolute Change at Week 52 (MMRM)		
n	266	248
LS mean (SE)	0.81 (0.22)	1.31 (0.23)
95% CI of LS mean	(0.38, 1.25)	(0.87, 1.76)
P-value within Treatment	0.0003	<0.0001
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-0.12, 1.12)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1140
Hedges' G (SE)		0.14 (0.09)
Hedges' 95% CI		(-0.03, 0.31)
Hedges' P-value		0.1145

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.6.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	59 (20.4)	61 (21.5)
Subjects Censored	230 (79.6)	223 (78.5)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9827 (0.9589, 0.9928)	0.9894 (0.9676, 0.9966)
4 Weeks	0.9689 (0.9410, 0.9837)	0.9789 (0.9536, 0.9905)
8 Weeks	0.9480 (0.9153, 0.9683)	0.9647 (0.9354, 0.9808)
12 Weeks	0.9272 (0.8905, 0.9519)	0.9255 (0.8880, 0.9508)
16 Weeks	0.9098 (0.8703, 0.9376)	0.8967 (0.8548, 0.9271)
24 Weeks	0.8817 (0.8384, 0.9140)	0.8567 (0.8098, 0.8928)
36 Weeks	0.8429 (0.7953, 0.8802)	0.8164 (0.7656, 0.8572)
52 Weeks	0.7916 (0.7392, 0.8346)	0.7829 (0.7295, 0.8271)
Hazard Ratio (95% CI)*	-	1.0762 (0.7494, 1.5456)
Two-sided P-value, superiority*	-	0.6909

-CI: Confidence interval.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
-Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
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Table 2.2.1.7.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	9 (3.1)	14 (4.9)
Subjects Censored	280 (96.9)	270 (95.1)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9965 (0.9753, 0.9995)
4 Weeks	0.9965 (0.9757, 0.9995)	0.9930 (0.9721, 0.9982)
8 Weeks	0.9965 (0.9757, 0.9995)	0.9930 (0.9721, 0.9982)
12 Weeks	0.9931 (0.9726, 0.9983)	0.9930 (0.9721, 0.9982)
16 Weeks	0.9931 (0.9726, 0.9983)	0.9858 (0.9626, 0.9946)
24 Weeks	0.9825 (0.9585, 0.9927)	0.9749 (0.9480, 0.9879)
36 Weeks	0.9755 (0.9493, 0.9882)	0.9529 (0.9203, 0.9724)
52 Weeks	0.9683 (0.9400, 0.9834)	0.9492 (0.9157, 0.9696)
Hazard Ratio (95% CI)*	-	1.4491 (0.6189, 3.3927)
Two-sided P-value, superiority*	-	0.3927

- CI: Confidence interval.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation requiring hospitalization during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).

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Table 2.2.1.8.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	17 (5.9)	19 (6.7)
Subjects Censored	272 (94.1)	265 (93.3)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9965 (0.9753, 0.9995)
4 Weeks	0.9931 (0.9726, 0.9983)	0.9930 (0.9721, 0.9982)
8 Weeks	0.9896 (0.9681, 0.9966)	0.9894 (0.9675, 0.9966)
12 Weeks	0.9792 (0.9543, 0.9906)	0.9858 (0.9627, 0.9947)
16 Weeks	0.9792 (0.9543, 0.9906)	0.9787 (0.9531, 0.9904)
24 Weeks	0.9616 (0.9318, 0.9786)	0.9605 (0.9298, 0.9779)
36 Weeks	0.9511 (0.9188, 0.9707)	0.9385 (0.9030, 0.9614)
52 Weeks	0.9403 (0.9058, 0.9625)	0.9311 (0.8942, 0.9555)
Hazard Ratio (95% CI)*	-	1.1021 (0.5609, 2.1653)
Two-sided P-value, superiority*	-	0.7779

- CI: Confidence interval.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation requiring IV Antibiotics during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).

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Table 2.2.1.9.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	282	280
Mean (SD)	85.62 (13.21)	85.71 (13.19)
Week 8 (MMRM)		
n	277	274
LS mean (SE)	85.12 (0.94)	84.70 (0.95)
95% CI of LS mean	(83.26, 86.97)	(82.84, 86.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.42 (-3.05, 2.21)
Absolute Change at Week 8 (MMRM)		
n	270	271
LS mean (SE)	-0.56 (0.99)	-1.20 (0.98)
95% CI of LS mean	(-2.50, 1.38)	(-3.14, 0.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-3.38, 2.10)
Week 16 (MMRM)		
n	272	268
LS mean (SE)	85.20 (0.97)	85.20 (0.98)
95% CI of LS mean	(83.30, 87.11)	(83.28, 87.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-2.71, 2.70)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	265	265
LS mean (SE)	-0.41 (0.96)	-0.64 (0.96)
95% CI of LS mean	(-2.30, 1.48)	(-2.53, 1.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-2.90, 2.45)
Week 24 (MMRM)		
n	274	265
LS mean (SE)	83.63 (0.93)	83.78 (0.94)
95% CI of LS mean	(81.81, 85.46)	(81.93, 85.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-2.45, 2.75)
Absolute Change at Week 24 (MMRM)		
n	267	262
LS mean (SE)	-1.98 (0.91)	-1.87 (0.92)
95% CI of LS mean	(-3.77, -0.19)	(-3.67, -0.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.11 (-2.43, 2.64)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Week 52		
n	277	264
Mean (SD)	84.88 (16.92)	87.24 (13.15)
Absolute Change at Week 52		
n	270	260
Mean (SD)	-0.79 (17.30)	1.55 (13.41)
Week 52 (MMRM)		
n	269	258
LS mean (SE)	84.91 (0.89)	87.09 (0.91)
95% CI of LS mean	(83.15, 86.66)	(85.30, 88.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.18 (-0.32, 4.69)
Absolute Change at Week 52 (MMRM)		
n	262	254
LS mean (SE)	-0.76 (0.96)	1.33 (0.97)
95% CI of LS mean	(-2.64, 1.13)	(-0.57, 3.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.09 (-0.59, 4.77)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	270	268
LS mean (SE)	-1.05 (0.74)	-0.39 (0.74)
95% CI of LS mean	(-2.50, 0.40)	(-1.85, 1.06)
P-value within Treatment	0.1545	0.5944
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.66 (-1.40, 2.71)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5303
Hedges' G (SE)		0.05 (0.09)
Hedges' 95% CI		(-0.12, 0.22)
Hedges' P-value		0.5302

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	282 (97.58)	280 (98.59)
Week 8	287 (99.31)	280 (98.59)
Absolute Change at Week 8	280 (96.89)	277 (97.54)
Week 16	282 (97.58)	274 (96.48)
Absolute Change at Week 16	275 (95.16)	271 (95.42)
Week 24	283 (97.92)	271 (95.42)
Absolute Change at Week 24	276 (95.50)	268 (94.37)
Week 52	277 (95.85)	264 (92.96)
Absolute Change at Week 52	270 (93.43)	260 (91.55)
Through Week 52	287 (99.31)	278 (97.89)
Absolute Change through Week 52	280 (96.89)	274 (96.48)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	282 (97.58)	280 (98.59)
Week 8	287 (99.31)	279 (98.24)
Absolute Change at Week 8	280 (96.89)	276 (97.18)
Week 16	283 (97.92)	273 (96.13)
Absolute Change at Week 16	276 (95.50)	270 (95.07)
Week 24	283 (97.92)	271 (95.42)
Absolute Change at Week 24	276 (95.50)	268 (94.37)
Week 52	277 (95.85)	265 (93.31)
Absolute Change at Week 52	270 (93.43)	261 (91.90)
Through Week 52	287 (99.31)	278 (97.89)
Absolute Change through Week 52	280 (96.89)	274 (96.48)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	282 (97.58)	280 (98.59)
Week 8	287 (99.31)	279 (98.24)
Absolute Change at Week 8	280 (96.89)	276 (97.18)
Week 16	282 (97.58)	274 (96.48)
Absolute Change at Week 16	275 (95.16)	271 (95.42)
Week 24	282 (97.58)	271 (95.42)
Absolute Change at Week 24	275 (95.16)	268 (94.37)
Week 52	277 (95.85)	264 (92.96)
Absolute Change at Week 52	270 (93.43)	260 (91.55)
Through Week 52	287 (99.31)	278 (97.89)
Absolute Change through Week 52	280 (96.89)	274 (96.48)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	282 (97.58)	280 (98.59)
Week 8	287 (99.31)	280 (98.59)
Absolute Change at Week 8	280 (96.89)	277 (97.54)
Week 16	283 (97.92)	274 (96.48)
Absolute Change at Week 16	276 (95.50)	271 (95.42)
Week 24	283 (97.92)	271 (95.42)
Absolute Change at Week 24	276 (95.50)	268 (94.37)
Week 52	277 (95.85)	265 (93.31)
Absolute Change at Week 52	270 (93.43)	261 (91.90)
Through Week 52	287 (99.31)	278 (97.89)
Absolute Change through Week 52	280 (96.89)	274 (96.48)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	282 (97.58)	280 (98.59)
Week 8	286 (98.96)	280 (98.59)
Absolute Change at Week 8	280 (96.89)	277 (97.54)
Week 16	283 (97.92)	274 (96.48)
Absolute Change at Week 16	276 (95.50)	271 (95.42)
Week 24	282 (97.58)	271 (95.42)
Absolute Change at Week 24	275 (95.16)	268 (94.37)
Week 52	277 (95.85)	265 (93.31)
Absolute Change at Week 52	270 (93.43)	261 (91.90)
Through Week 52	287 (99.31)	278 (97.89)
Absolute Change through Week 52	280 (96.89)	274 (96.48)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	269 (93.08)	266 (93.66)
Week 8	275 (95.16)	266 (93.66)
Absolute Change at Week 8	269 (93.08)	263 (92.61)
Week 16	271 (93.77)	260 (91.55)
Absolute Change at Week 16	265 (91.70)	257 (90.49)
Week 24	269 (93.08)	257 (90.49)
Absolute Change at Week 24	263 (91.00)	255 (89.79)
Week 52	266 (92.04)	251 (88.38)
Absolute Change at Week 52	260 (89.97)	248 (87.32)
Through Week 52	273 (94.46)	263 (92.61)
Absolute Change through Week 52	267 (92.39)	260 (91.55)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	282 (97.58)	280 (98.59)
Week 8	286 (98.96)	280 (98.59)
Absolute Change at Week 8	280 (96.89)	277 (97.54)
Week 16	283 (97.92)	274 (96.48)
Absolute Change at Week 16	276 (95.50)	271 (95.42)
Week 24	282 (97.58)	271 (95.42)
Absolute Change at Week 24	275 (95.16)	268 (94.37)
Week 52	277 (95.85)	265 (93.31)
Absolute Change at Week 52	270 (93.43)	261 (91.90)
Through Week 52	287 (99.31)	278 (97.89)
Absolute Change through Week 52	280 (96.89)	274 (96.48)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	269 (93.08)	266 (93.66)
Week 8	275 (95.16)	265 (93.31)
Absolute Change at Week 8	269 (93.08)	262 (92.25)
Week 16	269 (93.08)	261 (91.90)
Absolute Change at Week 16	263 (91.00)	258 (90.85)
Week 24	269 (93.08)	256 (90.14)
Absolute Change at Week 24	263 (91.00)	254 (89.44)
Week 52	266 (92.04)	250 (88.03)
Absolute Change at Week 52	260 (89.97)	247 (86.97)
Through Week 52	273 (94.46)	263 (92.61)
Absolute Change through Week 52	267 (92.39)	260 (91.55)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	282 (97.58)	280 (98.59)
Week 8	287 (99.31)	279 (98.24)
Absolute Change at Week 8	280 (96.89)	276 (97.18)
Week 16	283 (97.92)	273 (96.13)
Absolute Change at Week 16	276 (95.50)	270 (95.07)
Week 24	283 (97.92)	271 (95.42)
Absolute Change at Week 24	276 (95.50)	268 (94.37)
Week 52	277 (95.85)	265 (93.31)
Absolute Change at Week 52	270 (93.43)	261 (91.90)
Through Week 52	287 (99.31)	278 (97.89)
Absolute Change through Week 52	280 (96.89)	274 (96.48)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	282 (97.58)	280 (98.59)
Week 8	287 (99.31)	279 (98.24)
Absolute Change at Week 8	280 (96.89)	276 (97.18)
Week 16	283 (97.92)	274 (96.48)
Absolute Change at Week 16	276 (95.50)	271 (95.42)
Week 24	283 (97.92)	271 (95.42)
Absolute Change at Week 24	276 (95.50)	268 (94.37)
Week 52	277 (95.85)	265 (93.31)
Absolute Change at Week 52	270 (93.43)	261 (91.90)
Through Week 52	287 (99.31)	278 (97.89)
Absolute Change through Week 52	280 (96.89)	274 (96.48)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	269 (93.08)	266 (93.66)
Week 8	274 (94.81)	267 (94.01)
Absolute Change at Week 8	269 (93.08)	264 (92.96)
Week 16	271 (93.77)	261 (91.90)
Absolute Change at Week 16	265 (91.70)	258 (90.85)
Week 24	268 (92.73)	257 (90.49)
Absolute Change at Week 24	262 (90.66)	255 (89.79)
Week 52	266 (92.04)	251 (88.38)
Absolute Change at Week 52	260 (89.97)	248 (87.32)
Through Week 52	273 (94.46)	263 (92.61)
Absolute Change through Week 52	267 (92.39)	260 (91.55)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	266 (92.04)	266 (93.66)
Week 8	270 (93.43)	266 (93.66)
Absolute Change at Week 8	266 (92.04)	263 (92.61)
Week 16	264 (91.35)	261 (91.90)
Absolute Change at Week 16	260 (89.97)	258 (90.85)
Week 24	264 (91.35)	257 (90.49)
Absolute Change at Week 24	260 (89.97)	255 (89.79)
Week 52	266 (92.04)	250 (88.03)
Absolute Change at Week 52	257 (88.93)	247 (86.97)
Through Week 52	273 (94.46)	263 (92.61)
Absolute Change through Week 52	264 (91.35)	260 (91.55)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	94.81 (6.48)	90.65 (9.54)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	92.28 (2.77)	91.40 (2.54)
95% CI of LS mean	(86.50, 98.06)	(86.08, 96.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.88 (-8.79, 7.04)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	-0.89 (3.41)	-0.33 (2.94)
95% CI of LS mean	(-8.09, 6.31)	(-6.56, 5.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.56 (-8.99, 10.11)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	89.46 (4.78)	89.40 (4.37)
95% CI of LS mean	(79.50, 99.42)	(80.29, 98.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-13.59, 13.47)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	-3.41 (4.44)	-3.00 (3.63)
95% CI of LS mean	(-12.77, 5.94)	(-10.69, 4.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.41 (-11.77, 12.59)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	92.78 (5.42)	85.02 (5.14)
95% CI of LS mean	(81.59, 103.97)	(74.43, 95.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.75 (-23.20, 7.69)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	-0.86 (5.32)	-3.14 (5.10)
95% CI of LS mean	(-11.99, 10.27)	(-13.82, 7.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.28 (-17.74, 13.17)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Week 52		
n	11	13
Mean (SD)	96.26 (5.49)	94.87 (6.60)
Absolute Change at Week 52		
n	9	10
Mean (SD)	0.49 (6.90)	2.33 (7.56)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	96.26 (2.07)	95.20 (1.77)
95% CI of LS mean	(91.95, 100.56)	(91.50, 98.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.06 (-6.84, 4.72)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	1.83 (2.44)	1.47 (2.15)
95% CI of LS mean	(-3.31, 6.97)	(-3.06, 6.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.36 (-7.30, 6.58)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	-0.81 (2.44)	-1.56 (2.18)
95% CI of LS mean	(-5.95, 4.32)	(-6.17, 3.05)
P-value within Treatment	0.7427	0.4841
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.74 (-7.73, 6.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8249
Hedges' G (SE)		-0.09 (0.41)
Hedges' 95% CI		(-0.95, 0.77)
Hedges' P-value		0.8219

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	282	280
Mean (SD)	75.81 (23.65)	78.61 (21.40)
Week 8 (MMRM)		
n	277	273
LS mean (SE)	78.47 (1.33)	79.34 (1.34)
95% CI of LS mean	(75.85, 81.08)	(76.71, 81.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.87 (-2.84, 4.58)
Absolute Change at Week 8 (MMRM)		
n	270	270
LS mean (SE)	2.45 (0.89)	0.55 (0.88)
95% CI of LS mean	(0.71, 4.18)	(-1.19, 2.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.90 (-4.36, 0.56)
Week 16 (MMRM)		
n	273	267
LS mean (SE)	78.36 (1.25)	79.61 (1.26)
95% CI of LS mean	(75.90, 80.81)	(77.13, 82.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.25 (-2.24, 4.74)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	266	264
LS mean (SE)	2.13 (0.86)	0.68 (0.86)
95% CI of LS mean	(0.45, 3.82)	(-1.01, 2.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.45 (-3.84, 0.94)
Week 24 (MMRM)		
n	274	265
LS mean (SE)	79.19 (1.31)	79.76 (1.32)
95% CI of LS mean	(76.63, 81.76)	(77.18, 82.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.57 (-3.07, 4.21)
Absolute Change at Week 24 (MMRM)		
n	267	262
LS mean (SE)	3.13 (0.93)	0.96 (0.94)
95% CI of LS mean	(1.30, 4.96)	(-0.88, 2.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.17 (-4.76, 0.42)
Week 52		
n	277	265
Mean (SD)	78.62 (21.08)	79.58 (21.84)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52		
n	270	261
Mean (SD)	2.51 (17.07)	1.32 (16.47)
Week 52 (MMRM)		
n	269	259
LS mean (SE)	78.42 (1.29)	80.13 (1.30)
95% CI of LS mean	(75.89, 80.94)	(77.58, 82.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.71 (-1.88, 5.30)
Absolute Change at Week 52 (MMRM)		
n	262	255
LS mean (SE)	2.22 (1.03)	1.37 (1.04)
95% CI of LS mean	(0.19, 4.26)	(-0.68, 3.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.85 (-3.74, 2.04)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	270	268
LS mean (SE)	2.50 (0.79)	1.00 (0.80)
95% CI of LS mean	(0.94, 4.05)	(-0.56, 2.57)
P-value within Treatment	0.0017	0.2073
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.49 (-3.70, 0.72)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1848
Hedges' G (SE)		-0.11 (0.09)
Hedges' 95% CI		(-0.28, 0.05)
Hedges' P-value		0.1849

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	282	280
Mean (SD)	81.09 (17.14)	82.06 (18.39)
Week 8 (MMRM)		
n	277	273
LS mean (SE)	81.18 (1.11)	81.30 (1.12)
95% CI of LS mean	(78.99, 83.37)	(79.10, 83.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-2.99, 3.22)
Absolute Change at Week 8 (MMRM)		
n	270	270
LS mean (SE)	0.14 (0.89)	-0.70 (0.89)
95% CI of LS mean	(-1.60, 1.89)	(-2.44, 1.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.84 (-3.31, 1.62)
Week 16 (MMRM)		
n	272	268
LS mean (SE)	80.83 (1.11)	81.29 (1.12)
95% CI of LS mean	(78.64, 83.01)	(79.09, 83.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.46 (-2.64, 3.57)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	265	265
LS mean (SE)	-0.18 (0.92)	-0.82 (0.92)
95% CI of LS mean	(-1.99, 1.63)	(-2.63, 0.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-3.20, 1.92)
Week 24 (MMRM)		
n	273	265
LS mean (SE)	80.96 (1.16)	80.15 (1.17)
95% CI of LS mean	(78.67, 83.24)	(77.84, 82.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.81 (-4.05, 2.44)
Absolute Change at Week 24 (MMRM)		
n	266	262
LS mean (SE)	0.06 (0.92)	-1.97 (0.92)
95% CI of LS mean	(-1.74, 1.85)	(-3.78, -0.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.03 (-4.58, 0.52)
Week 52		
n	277	264
Mean (SD)	79.58 (20.30)	79.80 (19.08)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52		
n	270	260
Mean (SD)	-1.48 (15.73)	-2.44 (16.14)
Week 52 (MMRM)		
n	269	258
LS mean (SE)	79.10 (1.19)	80.03 (1.20)
95% CI of LS mean	(76.77, 81.44)	(77.66, 82.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.92 (-2.41, 4.25)
Absolute Change at Week 52 (MMRM)		
n	262	254
LS mean (SE)	-1.90 (0.99)	-2.09 (1.00)
95% CI of LS mean	(-3.83, 0.04)	(-4.05, -0.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.20 (-2.95, 2.55)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	270	268
LS mean (SE)	-0.67 (0.79)	-1.63 (0.79)
95% CI of LS mean	(-2.23, 0.88)	(-3.19, -0.07)
P-value within Treatment	0.3943	0.0404
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.96 (-3.15, 1.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3939
Hedges' G (SE)		-0.07 (0.09)
Hedges' 95% CI		(-0.24, 0.10)
Hedges' P-value		0.3938

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	282	280
Mean (SD)	92.77 (14.46)	94.23 (11.95)
Week 8 (MMRM)		
n	277	274
LS mean (SE)	92.56 (0.82)	94.04 (0.83)
95% CI of LS mean	(90.94, 94.18)	(92.41, 95.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.48 (-0.82, 3.78)
Absolute Change at Week 8 (MMRM)		
n	270	271
LS mean (SE)	0.16 (0.66)	-0.15 (0.66)
95% CI of LS mean	(-1.14, 1.46)	(-1.45, 1.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-2.15, 1.53)
Week 16 (MMRM)		
n	273	268
LS mean (SE)	92.65 (0.87)	93.15 (0.88)
95% CI of LS mean	(90.93, 94.36)	(91.42, 94.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-1.94, 2.93)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	266	265
LS mean (SE)	0.26 (0.72)	-1.06 (0.73)
95% CI of LS mean	(-1.16, 1.68)	(-2.48, 0.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.32 (-3.33, 0.70)
Week 24 (MMRM)		
n	274	265
LS mean (SE)	92.50 (0.93)	92.55 (0.94)
95% CI of LS mean	(90.68, 94.32)	(90.71, 94.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-2.54, 2.64)
Absolute Change at Week 24 (MMRM)		
n	267	262
LS mean (SE)	0.03 (0.75)	-1.67 (0.75)
95% CI of LS mean	(-1.44, 1.50)	(-3.15, -0.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.70 (-3.78, 0.39)
Week 52		
n	277	265
Mean (SD)	92.94 (14.93)	93.38 (13.50)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52		
n	270	261
Mean (SD)	0.47 (13.29)	-1.04 (11.45)
Week 52 (MMRM)		
n	269	259
LS mean (SE)	92.89 (0.86)	93.41 (0.87)
95% CI of LS mean	(91.20, 94.57)	(91.71, 95.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.53 (-1.87, 2.93)
Absolute Change at Week 52 (MMRM)		
n	262	255
LS mean (SE)	0.36 (0.76)	-0.80 (0.77)
95% CI of LS mean	(-1.14, 1.86)	(-2.31, 0.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.16 (-3.30, 0.98)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	270	268
LS mean (SE)	0.22 (0.59)	-1.17 (0.59)
95% CI of LS mean	(-0.93, 1.37)	(-2.33, -0.02)
P-value within Treatment	0.7116	0.0462
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.39 (-3.02, 0.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0943
Hedges' G (SE)		-0.14 (0.09)
Hedges' 95% CI		(-0.31, 0.02)
Hedges' P-value		0.0946

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	282	280
Mean (SD)	81.81 (16.33)	81.75 (17.76)
Week 8 (MMRM)		
n	276	274
LS mean (SE)	82.27 (1.02)	82.90 (1.02)
95% CI of LS mean	(80.27, 84.27)	(80.89, 84.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-2.20, 3.46)
Absolute Change at Week 8 (MMRM)		
n	270	271
LS mean (SE)	0.64 (0.68)	1.09 (0.68)
95% CI of LS mean	(-0.70, 1.98)	(-0.25, 2.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-1.45, 2.34)
Week 16 (MMRM)		
n	273	268
LS mean (SE)	82.45 (1.03)	81.22 (1.03)
95% CI of LS mean	(80.43, 84.47)	(79.19, 83.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.23 (-4.09, 1.63)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	266	265
LS mean (SE)	1.01 (0.72)	-0.55 (0.72)
95% CI of LS mean	(-0.40, 2.42)	(-1.96, 0.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.56 (-3.55, 0.44)
Week 24 (MMRM)		
n	273	265
LS mean (SE)	81.68 (1.05)	81.19 (1.06)
95% CI of LS mean	(79.62, 83.73)	(79.12, 83.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.48 (-3.40, 2.44)
Absolute Change at Week 24 (MMRM)		
n	266	262
LS mean (SE)	0.07 (0.77)	-0.62 (0.77)
95% CI of LS mean	(-1.44, 1.58)	(-2.14, 0.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.69 (-2.83, 1.45)
Week 52		
n	277	265
Mean (SD)	81.69 (16.98)	81.90 (18.26)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52		
n	270	261
Mean (SD)	-0.36 (14.00)	0.34 (14.62)
Week 52 (MMRM)		
n	269	259
LS mean (SE)	81.38 (1.07)	81.81 (1.08)
95% CI of LS mean	(79.29, 83.47)	(79.69, 83.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-2.55, 3.41)
Absolute Change at Week 52 (MMRM)		
n	262	255
LS mean (SE)	-0.34 (0.88)	0.09 (0.89)
95% CI of LS mean	(-2.07, 1.39)	(-1.66, 1.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-2.03, 2.88)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	270	268
LS mean (SE)	0.25 (0.66)	-0.36 (0.66)
95% CI of LS mean	(-1.06, 1.55)	(-1.67, 0.95)
P-value within Treatment	0.7106	0.5878
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.61 (-2.45, 1.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5186
Hedges' G (SE)		-0.06 (0.09)
Hedges' 95% CI		(-0.22, 0.11)
Hedges' P-value		0.5185

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	269	266
Mean (SD)	71.46 (19.62)	72.79 (20.06)
Week 8 (MMRM)		
n	267	260
LS mean (SE)	71.38 (1.19)	71.87 (1.20)
95% CI of LS mean	(69.04, 73.72)	(69.50, 74.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-2.84, 3.83)
Absolute Change at Week 8 (MMRM)		
n	261	257
LS mean (SE)	0.00 (0.90)	-1.06 (0.91)
95% CI of LS mean	(-1.77, 1.77)	(-2.84, 0.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.06 (-3.58, 1.45)
Week 16 (MMRM)		
n	263	254
LS mean (SE)	71.13 (1.19)	71.94 (1.21)
95% CI of LS mean	(68.79, 73.47)	(69.57, 74.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.81 (-2.52, 4.14)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	257	251
LS mean (SE)	0.03 (0.94)	-1.04 (0.95)
95% CI of LS mean	(-1.83, 1.88)	(-2.91, 0.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.07 (-3.70, 1.57)
Week 24 (MMRM)		
n	262	251
LS mean (SE)	69.67 (1.27)	72.07 (1.29)
95% CI of LS mean	(67.18, 72.17)	(69.53, 74.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.39 (-1.16, 5.95)
Absolute Change at Week 24 (MMRM)		
n	256	249
LS mean (SE)	-1.46 (1.01)	-0.90 (1.02)
95% CI of LS mean	(-3.45, 0.53)	(-2.91, 1.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.57 (-2.27, 3.40)
Week 52		
n	266	251
Mean (SD)	73.98 (19.45)	73.40 (19.65)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52		
n	260	248
Mean (SD)	2.39 (15.83)	0.47 (14.83)
Week 52 (MMRM)		
n	259	245
LS mean (SE)	73.64 (1.19)	73.10 (1.21)
95% CI of LS mean	(71.30, 75.97)	(70.72, 75.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.53 (-3.87, 2.81)
Absolute Change at Week 52 (MMRM)		
n	253	242
LS mean (SE)	2.31 (0.97)	0.20 (0.99)
95% CI of LS mean	(0.40, 4.21)	(-1.74, 2.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.11 (-4.83, 0.61)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	259	254
LS mean (SE)	0.29 (0.79)	-0.58 (0.80)
95% CI of LS mean	(-1.26, 1.84)	(-2.14, 0.99)
P-value within Treatment	0.7128	0.4688
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.87 (-3.07, 1.34)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4393
Hedges' G (SE)		-0.07 (0.09)
Hedges' 95% CI		(-0.24, 0.11)
Hedges' P-value		0.4392

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	282	280
Mean (SD)	80.66 (20.30)	82.83 (18.60)
Week 8 (MMRM)		
n	276	274
LS mean (SE)	80.20 (1.20)	82.18 (1.20)
95% CI of LS mean	(77.85, 82.55)	(79.83, 84.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.98 (-1.35, 5.31)
Absolute Change at Week 8 (MMRM)		
n	270	271
LS mean (SE)	-0.60 (0.95)	-0.85 (0.95)
95% CI of LS mean	(-2.47, 1.27)	(-2.72, 1.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-2.90, 2.39)
Week 16 (MMRM)		
n	273	268
LS mean (SE)	81.34 (1.18)	82.60 (1.19)
95% CI of LS mean	(79.02, 83.67)	(80.26, 84.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.26 (-2.04, 4.56)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	266	265
LS mean (SE)	0.80 (0.92)	-0.33 (0.92)
95% CI of LS mean	(-1.00, 2.60)	(-2.13, 1.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.13 (-3.67, 1.42)
Week 24 (MMRM)		
n	273	265
LS mean (SE)	80.42 (1.21)	82.12 (1.22)
95% CI of LS mean	(78.05, 82.80)	(79.72, 84.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.69 (-1.69, 5.07)
Absolute Change at Week 24 (MMRM)		
n	266	262
LS mean (SE)	-0.35 (0.91)	-0.68 (0.91)
95% CI of LS mean	(-2.14, 1.44)	(-2.48, 1.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-2.87, 2.20)
Week 52		
n	277	265
Mean (SD)	81.43 (20.38)	84.37 (18.25)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52		
n	270	261
Mean (SD)	1.03 (16.44)	1.42 (12.43)
Week 52 (MMRM)		
n	269	259
LS mean (SE)	81.63 (1.12)	84.00 (1.13)
95% CI of LS mean	(79.43, 83.82)	(81.78, 86.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.37 (-0.75, 5.50)
Absolute Change at Week 52 (MMRM)		
n	262	255
LS mean (SE)	0.98 (0.90)	1.11 (0.91)
95% CI of LS mean	(-0.79, 2.75)	(-0.68, 2.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-2.38, 2.64)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	270	268
LS mean (SE)	0.48 (0.73)	0.03 (0.73)
95% CI of LS mean	(-0.95, 1.90)	(-1.40, 1.46)
P-value within Treatment	0.5125	0.9659
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.44 (-2.47, 1.58)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6659
Hedges' G (SE)		-0.04 (0.09)
Hedges' 95% CI		(-0.21, 0.13)
Hedges' P-value		0.6658

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	269	266
Mean (SD)	86.65 (15.63)	86.75 (16.40)
Week 8 (MMRM)		
n	267	259
LS mean (SE)	86.39 (0.98)	87.43 (0.99)
95% CI of LS mean	(84.47, 88.31)	(85.49, 89.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.04 (-1.70, 3.78)
Absolute Change at Week 8 (MMRM)		
n	261	256
LS mean (SE)	-0.21 (0.83)	0.60 (0.83)
95% CI of LS mean	(-1.83, 1.42)	(-1.03, 2.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.81 (-1.50, 3.11)
Week 16 (MMRM)		
n	261	255
LS mean (SE)	86.56 (1.01)	86.74 (1.02)
95% CI of LS mean	(84.58, 88.54)	(84.74, 88.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-2.64, 3.00)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	255	252
LS mean (SE)	0.02 (0.86)	0.04 (0.86)
95% CI of LS mean	(-1.67, 1.71)	(-1.66, 1.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.02 (-2.38, 2.41)
Week 24 (MMRM)		
n	262	250
LS mean (SE)	85.95 (1.06)	86.35 (1.08)
95% CI of LS mean	(83.87, 88.02)	(84.24, 88.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.41 (-2.56, 3.37)
Absolute Change at Week 24 (MMRM)		
n	256	248
LS mean (SE)	-0.57 (0.96)	-0.36 (0.97)
95% CI of LS mean	(-2.46, 1.31)	(-2.26, 1.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.22 (-2.46, 2.90)
Week 52		
n	266	250
Mean (SD)	87.14 (17.10)	88.97 (14.04)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52		
n	260	247
Mean (SD)	0.63 (15.08)	1.65 (13.31)
Week 52 (MMRM)		
n	259	244
LS mean (SE)	87.08 (0.97)	88.76 (1.00)
95% CI of LS mean	(85.17, 89.00)	(86.81, 90.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.68 (-1.06, 4.42)
Absolute Change at Week 52 (MMRM)		
n	253	241
LS mean (SE)	0.43 (0.89)	1.95 (0.91)
95% CI of LS mean	(-1.33, 2.18)	(0.16, 3.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.53 (-0.98, 4.04)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	259	254
LS mean (SE)	-0.04 (0.73)	0.54 (0.74)
95% CI of LS mean	(-1.48, 1.39)	(-0.90, 1.99)
P-value within Treatment	0.9530	0.4610
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.59 (-1.45, 2.63)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5719
Hedges' G (SE)		0.05 (0.09)
Hedges' 95% CI		(-0.12, 0.22)
Hedges' P-value		0.5718

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	282	280
Mean (SD)	72.51 (17.81)	75.03 (17.85)
Week 8 (MMRM)		
n	277	273
LS mean (SE)	73.78 (1.05)	75.71 (1.06)
95% CI of LS mean	(71.72, 75.84)	(73.64, 77.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.93 (-1.00, 4.85)
Absolute Change at Week 8 (MMRM)		
n	270	270
LS mean (SE)	0.87 (0.83)	0.48 (0.83)
95% CI of LS mean	(-0.76, 2.49)	(-1.15, 2.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.39 (-2.69, 1.91)
Week 16 (MMRM)		
n	273	267
LS mean (SE)	74.64 (1.05)	76.13 (1.06)
95% CI of LS mean	(72.58, 76.71)	(74.05, 78.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.49 (-1.45, 4.43)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	266	264
LS mean (SE)	1.97 (0.85)	0.98 (0.85)
95% CI of LS mean	(0.29, 3.64)	(-0.70, 2.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.99 (-3.36, 1.38)
Week 24 (MMRM)		
n	274	265
LS mean (SE)	73.47 (1.05)	77.23 (1.06)
95% CI of LS mean	(71.42, 75.53)	(75.15, 79.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.76 (0.83, 6.68)
Absolute Change at Week 24 (MMRM)		
n	267	262
LS mean (SE)	0.72 (0.86)	2.11 (0.86)
95% CI of LS mean	(-0.96, 2.41)	(0.41, 3.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.39 (-1.00, 3.78)
Week 52		
n	277	265
Mean (SD)	76.49 (18.05)	79.58 (17.54)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52		
n	270	261
Mean (SD)	4.08 (14.62)	4.29 (13.87)
Week 52 (MMRM)		
n	269	259
LS mean (SE)	76.41 (1.06)	79.35 (1.07)
95% CI of LS mean	(74.32, 78.49)	(77.24, 81.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.94 (-0.02, 5.91)
Absolute Change at Week 52 (MMRM)		
n	262	255
LS mean (SE)	3.64 (0.88)	4.19 (0.88)
95% CI of LS mean	(1.92, 5.36)	(2.45, 5.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.55 (-1.89, 2.99)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	270	268
LS mean (SE)	2.11 (0.72)	2.42 (0.72)
95% CI of LS mean	(0.70, 3.52)	(1.01, 3.84)
P-value within Treatment	0.0035	0.0008
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.32 (-1.69, 2.32)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7569
Hedges' G (SE)		0.03 (0.09)
Hedges' 95% CI		(-0.14, 0.20)
Hedges' P-value		0.7567

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	282	280
Mean (SD)	70.33 (19.73)	71.67 (19.06)
Week 8 (MMRM)		
n	277	273
LS mean (SE)	70.72 (1.20)	73.47 (1.20)
95% CI of LS mean	(68.38, 73.07)	(71.11, 75.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.75 (-0.58, 6.08)
Absolute Change at Week 8 (MMRM)		
n	270	270
LS mean (SE)	0.82 (0.84)	1.77 (0.84)
95% CI of LS mean	(-0.83, 2.47)	(0.12, 3.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.95 (-1.38, 3.29)
Week 16 (MMRM)		
n	273	268
LS mean (SE)	71.79 (1.18)	73.38 (1.19)
95% CI of LS mean	(69.47, 74.11)	(71.04, 75.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.59 (-1.71, 4.88)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	266	265
LS mean (SE)	1.96 (0.88)	1.67 (0.88)
95% CI of LS mean	(0.24, 3.68)	(-0.05, 3.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.29 (-2.72, 2.15)
Week 24 (MMRM)		
n	274	265
LS mean (SE)	70.67 (1.21)	73.68 (1.22)
95% CI of LS mean	(68.29, 73.05)	(71.29, 76.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.01 (-0.36, 6.39)
Absolute Change at Week 24 (MMRM)		
n	267	262
LS mean (SE)	0.92 (0.89)	1.98 (0.90)
95% CI of LS mean	(-0.83, 2.67)	(0.22, 3.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.06 (-1.42, 3.55)
Week 52		
n	277	265
Mean (SD)	73.49 (19.93)	75.93 (19.33)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52		
n	270	261
Mean (SD)	3.37 (16.58)	4.38 (15.26)
Week 52 (MMRM)		
n	269	259
LS mean (SE)	73.32 (1.18)	75.77 (1.19)
95% CI of LS mean	(71.00, 75.63)	(73.43, 78.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.45 (-0.84, 5.74)
Absolute Change at Week 52 (MMRM)		
n	262	255
LS mean (SE)	3.50 (0.99)	4.08 (0.99)
95% CI of LS mean	(1.56, 5.44)	(2.13, 6.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-2.17, 3.34)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	270	268
LS mean (SE)	2.13 (0.78)	2.58 (0.78)
95% CI of LS mean	(0.60, 3.65)	(1.05, 4.11)
P-value within Treatment	0.0064	0.0010
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-1.71, 2.61)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6799
Hedges' G (SE)		0.04 (0.09)
Hedges' 95% CI		(-0.13, 0.20)
Hedges' P-value		0.6797

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	269	266
Mean (SD)	66.76 (19.04)	66.82 (18.90)
Week 8 (MMRM)		
n	266	261
LS mean (SE)	63.99 (1.25)	66.46 (1.26)
95% CI of LS mean	(61.53, 66.45)	(63.98, 68.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.47 (-1.02, 5.96)
Absolute Change at Week 8 (MMRM)		
n	261	258
LS mean (SE)	-2.38 (1.00)	-0.46 (1.01)
95% CI of LS mean	(-4.34, -0.41)	(-2.44, 1.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.91 (-0.87, 4.70)
Week 16 (MMRM)		
n	263	255
LS mean (SE)	63.83 (1.24)	65.62 (1.26)
95% CI of LS mean	(61.40, 66.27)	(63.15, 68.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.78 (-1.68, 5.25)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	257	252
LS mean (SE)	-2.35 (0.97)	-1.26 (0.97)
95% CI of LS mean	(-4.24, -0.45)	(-3.17, 0.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.09 (-1.61, 3.78)
Week 24 (MMRM)		
n	261	251
LS mean (SE)	62.81 (1.28)	64.72 (1.30)
95% CI of LS mean	(60.30, 65.32)	(62.17, 67.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.91 (-1.67, 5.49)
Absolute Change at Week 24 (MMRM)		
n	255	249
LS mean (SE)	-3.74 (1.06)	-2.16 (1.07)
95% CI of LS mean	(-5.81, -1.66)	(-4.26, -0.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.57 (-1.38, 4.53)
Week 52		
n	266	251
Mean (SD)	64.94 (19.94)	67.66 (18.44)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52		
n	260	248
Mean (SD)	-1.47 (16.26)	0.54 (15.12)
Week 52 (MMRM)		
n	259	245
LS mean (SE)	64.54 (1.17)	66.92 (1.20)
95% CI of LS mean	(62.23, 66.85)	(64.57, 69.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-0.91, 5.68)
Absolute Change at Week 52 (MMRM)		
n	253	242
LS mean (SE)	-1.79 (0.99)	0.07 (1.00)
95% CI of LS mean	(-3.73, 0.14)	(-1.90, 2.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.87 (-0.90, 4.63)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	259	254
LS mean (SE)	-2.63 (0.81)	-1.12 (0.82)
95% CI of LS mean	(-4.21, -1.04)	(-2.72, 0.49)
P-value within Treatment	0.0012	0.1717
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.51 (-0.75, 3.77)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1897
Hedges' G (SE)		0.12 (0.09)
Hedges' 95% CI		(-0.06, 0.29)
Hedges' P-value		0.1898

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	266	266
Mean (SD)	88.47 (24.07)	84.34 (27.03)
Week 8 (MMRM)		
n	262	260
LS mean (SE)	87.25 (1.63)	84.91 (1.64)
95% CI of LS mean	(84.04, 90.46)	(81.68, 88.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.34 (-6.89, 2.21)
Absolute Change at Week 8 (MMRM)		
n	258	257
LS mean (SE)	-1.63 (1.29)	0.40 (1.29)
95% CI of LS mean	(-4.17, 0.90)	(-2.13, 2.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.03 (-1.55, 5.62)
Week 16 (MMRM)		
n	257	255
LS mean (SE)	86.33 (1.69)	85.77 (1.70)
95% CI of LS mean	(83.01, 89.65)	(82.43, 89.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.56 (-5.27, 4.15)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	253	252
LS mean (SE)	-2.56 (1.41)	1.27 (1.42)
95% CI of LS mean	(-5.34, 0.21)	(-1.51, 4.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.84 (-0.09, 7.77)
Week 24 (MMRM)		
n	257	251
LS mean (SE)	86.14 (1.71)	85.26 (1.73)
95% CI of LS mean	(82.79, 89.50)	(81.87, 88.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.88 (-5.65, 3.90)
Absolute Change at Week 24 (MMRM)		
n	253	249
LS mean (SE)	-2.61 (1.31)	0.91 (1.32)
95% CI of LS mean	(-5.19, -0.03)	(-1.69, 3.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.52 (-0.15, 7.18)
Week 52		
n	266	250
Mean (SD)	87.09 (26.31)	84.27 (28.05)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52		
n	257	247
Mean (SD)	-1.82 (22.56)	-0.13 (22.19)
Week 52 (MMRM)		
n	259	244
LS mean (SE)	86.64 (1.67)	84.25 (1.70)
95% CI of LS mean	(83.35, 89.92)	(80.90, 87.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.39 (-7.08, 2.30)
Absolute Change at Week 52 (MMRM)		
n	250	241
LS mean (SE)	-2.24 (1.42)	-0.11 (1.44)
95% CI of LS mean	(-5.03, 0.56)	(-2.94, 2.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.13 (-1.85, 6.11)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	256	254
LS mean (SE)	-2.47 (1.14)	0.69 (1.15)
95% CI of LS mean	(-4.72, -0.22)	(-1.56, 2.95)
P-value within Treatment	0.0313	0.5472
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.16 (-0.02, 6.34)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0517
Hedges' G (SE)		0.17 (0.09)
Hedges' 95% CI		(0.00, 0.35)
Hedges' P-value		0.0520

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	79.63 (23.61)	86.11 (17.81)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	74.53 (6.62)	91.67 (6.00)
95% CI of LS mean	(60.79, 88.27)	(79.20, 104.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	17.14 (-1.53, 35.81)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	-4.27 (6.01)	2.68 (5.06)
95% CI of LS mean	(-16.94, 8.40)	(-8.00, 13.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.95 (-9.82, 23.72)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	79.91 (3.99)	95.71 (3.56)
95% CI of LS mean	(71.59, 88.22)	(88.29, 103.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	15.81 (4.43, 27.18)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	2.78 (6.47)	11.92 (5.87)
95% CI of LS mean	(-10.81, 16.37)	(-0.41, 24.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.14 (-9.29, 27.57)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	77.95 (4.92)	91.32 (4.59)
95% CI of LS mean	(67.76, 88.13)	(81.84, 100.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	13.37 (-0.70, 27.45)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	0.07 (5.53)	8.47 (5.16)
95% CI of LS mean	(-11.53, 11.66)	(-2.32, 19.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.40 (-7.58, 24.39)
Week 52		
n	11	13
Mean (SD)	91.92 (15.78)	91.45 (11.25)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	6.17 (20.12)	4.44 (13.04)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	84.66 (4.89)	94.15 (4.34)
95% CI of LS mean	(74.46, 94.85)	(85.09, 103.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.49 (-4.31, 23.30)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	5.74 (6.57)	8.97 (5.88)
95% CI of LS mean	(-8.20, 19.68)	(-3.53, 21.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.23 (-15.67, 22.13)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	2.86 (5.60)	9.79 (5.11)
95% CI of LS mean	(-8.92, 14.65)	(-0.97, 20.54)
P-value within Treatment	0.6156	0.0719
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.92 (-9.19, 23.04)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3780
Hedges' G (SE)		0.38 (0.42)
Hedges' 95% CI		(-0.49, 1.24)
Hedges' P-value		0.3762

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	82.41 (17.38)	87.96 (10.00)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	79.61 (4.98)	86.27 (4.47)
95% CI of LS mean	(69.29, 89.93)	(77.02, 95.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.66 (-7.41, 20.73)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	1.11 (3.87)	-2.59 (3.35)
95% CI of LS mean	(-6.99, 9.21)	(-9.64, 4.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.70 (-14.58, 7.17)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	75.56 (4.96)	85.65 (4.44)
95% CI of LS mean	(65.26, 85.86)	(76.40, 94.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.09 (-3.98, 24.16)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	-4.91 (4.66)	-5.33 (3.82)
95% CI of LS mean	(-14.72, 4.90)	(-13.45, 2.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.42 (-13.31, 12.46)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	73.90 (5.51)	93.11 (5.10)
95% CI of LS mean	(62.51, 85.30)	(82.58, 103.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	19.21 (3.50, 34.91)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	-7.18 (4.58)	2.72 (4.34)
95% CI of LS mean	(-16.79, 2.43)	(-6.39, 11.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.90 (-3.44, 23.24)
Week 52		
n	11	13
Mean (SD)	82.83 (14.37)	84.62 (13.25)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	-4.94 (9.80)	-1.11 (8.20)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	72.58 (5.24)	85.33 (4.61)
95% CI of LS mean	(61.57, 83.59)	(75.60, 95.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	12.75 (-2.16, 27.65)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	-9.38 (4.40)	-2.82 (3.92)
95% CI of LS mean	(-19.18, 0.41)	(-11.64, 5.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.56 (-6.72, 19.84)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	-7.16 (3.34)	-1.81 (2.99)
95% CI of LS mean	(-14.20, -0.11)	(-8.15, 4.53)
P-value within Treatment	0.0468	0.5529
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.35 (-4.31, 15.00)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2585
Hedges' G (SE)		0.49 (0.42)
Hedges' 95% CI		(-0.38, 1.37)
Hedges' P-value		0.2531

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	94.44 (14.79)	91.67 (15.08)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	87.02 (4.90)	96.44 (4.55)
95% CI of LS mean	(76.92, 97.11)	(87.05, 105.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.42 (-4.43, 23.26)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	-6.50 (3.54)	5.57 (3.08)
95% CI of LS mean	(-13.96, 0.95)	(-0.95, 12.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	12.07 (2.12, 22.02)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	93.31 (4.13)	96.64 (3.87)
95% CI of LS mean	(84.76, 101.86)	(88.62, 104.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.33 (-8.46, 15.12)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	-2.50 (2.21)	4.24 (1.97)
95% CI of LS mean	(-7.12, 2.11)	(0.11, 8.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.74 (0.47, 13.02)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	91.77 (3.77)	96.46 (3.55)
95% CI of LS mean	(83.97, 99.57)	(89.12, 103.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.69 (-6.10, 15.48)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	-2.00 (2.94)	6.17 (2.72)
95% CI of LS mean	(-8.16, 4.15)	(0.49, 11.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.18 (-0.25, 16.61)
Week 52		
n	11	13
Mean (SD)	100.00 (0.00)	96.15 (9.99)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	0.00 (0.00)	-1.67 (14.59)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	99.48 (2.83)	95.36 (2.36)
95% CI of LS mean	(93.16, 105.81)	(90.03, 100.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.13 (-12.60, 4.35)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	-2.89 (5.13)	1.62 (4.64)
95% CI of LS mean	(-14.47, 8.68)	(-8.89, 12.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.51 (-11.14, 20.16)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	-2.47 (3.19)	4.01 (2.91)
95% CI of LS mean	(-9.35, 4.41)	(-2.26, 10.27)
P-value within Treatment	0.4533	0.1905
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.48 (-2.87, 15.82)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1590
Hedges' G (SE)		0.62 (0.42)
Hedges' 95% CI		(-0.26, 1.50)
Hedges' P-value		0.1590

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	82.22 (16.41)	79.44 (18.74)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	85.32 (3.63)	89.11 (3.27)
95% CI of LS mean	(77.75, 92.90)	(82.27, 95.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.78 (-6.56, 14.13)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	5.51 (4.90)	10.50 (4.35)
95% CI of LS mean	(-4.80, 15.81)	(1.32, 19.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.00 (-9.07, 19.06)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	82.87 (4.91)	84.69 (4.44)
95% CI of LS mean	(72.51, 93.23)	(75.32, 94.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.82 (-12.24, 15.88)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	4.41 (4.62)	5.76 (3.98)
95% CI of LS mean	(-5.27, 14.10)	(-2.65, 14.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.35 (-11.81, 14.51)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	81.63 (4.88)	86.71 (4.47)
95% CI of LS mean	(71.54, 91.72)	(77.49, 95.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.08 (-8.69, 18.85)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	1.75 (4.95)	8.50 (4.56)
95% CI of LS mean	(-8.64, 12.14)	(-1.06, 18.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.75 (-7.62, 21.12)
Week 52		
n	11	13
Mean (SD)	84.85 (12.33)	81.54 (12.22)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	0.00 (15.99)	-2.00 (12.98)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	82.81 (3.65)	81.82 (3.18)
95% CI of LS mean	(75.30, 90.32)	(75.26, 88.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.99 (-11.12, 9.14)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	0.83 (5.71)	2.64 (5.16)
95% CI of LS mean	(-11.93, 13.59)	(-8.96, 14.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.81 (-15.58, 19.19)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	2.33 (4.57)	5.63 (4.14)
95% CI of LS mean	(-7.42, 12.08)	(-3.21, 14.48)
P-value within Treatment	0.6175	0.1943
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.30 (-10.14, 16.74)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6082
Hedges' G (SE)		0.22 (0.41)
Hedges' 95% CI		(-0.64, 1.08)
Hedges' P-value		0.5993

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	79.63 (14.08)	75.93 (24.08)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	74.55 (5.74)	80.78 (5.19)
95% CI of LS mean	(62.57, 86.53)	(69.93, 91.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.22 (-10.07, 22.52)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	-5.19 (6.85)	7.73 (5.92)
95% CI of LS mean	(-19.47, 9.10)	(-4.69, 20.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	12.92 (-6.22, 32.06)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	75.12 (6.06)	74.79 (5.36)
95% CI of LS mean	(62.46, 87.78)	(63.54, 86.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-17.40, 16.74)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	-2.45 (6.33)	-2.59 (5.10)
95% CI of LS mean	(-15.80, 10.90)	(-13.45, 8.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-17.66, 17.39)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	79.60 (4.59)	82.77 (4.22)
95% CI of LS mean	(70.08, 89.12)	(74.03, 91.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.17 (-9.93, 16.27)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	1.02 (6.63)	7.77 (6.12)
95% CI of LS mean	(-12.87, 14.90)	(-5.03, 20.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.75 (-12.33, 25.83)
Week 52		
n	11	13
Mean (SD)	86.87 (10.91)	81.20 (17.20)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	2.47 (13.35)	-2.22 (20.82)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	84.94 (4.65)	81.41 (4.09)
95% CI of LS mean	(75.33, 94.56)	(72.93, 89.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.54 (-16.54, 9.47)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	6.16 (7.39)	5.05 (6.70)
95% CI of LS mean	(-9.61, 21.94)	(-9.28, 19.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.11 (-22.57, 20.35)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	1.58 (5.73)	3.41 (5.13)
95% CI of LS mean	(-10.44, 13.60)	(-7.38, 14.20)
P-value within Treatment	0.7863	0.5146
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.83 (-14.59, 18.25)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8173
Hedges' G (SE)		0.10 (0.41)
Hedges' 95% CI		(-0.76, 0.96)
Hedges' P-value		0.8137

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	86.11 (14.36)	85.42 (20.98)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	91.77 (3.30)	92.67 (2.99)
95% CI of LS mean	(84.94, 98.61)	(86.48, 98.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.90 (-8.51, 10.30)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	6.67 (4.19)	5.68 (3.79)
95% CI of LS mean	(-2.12, 15.47)	(-2.30, 13.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.00 (-13.08, 11.09)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	89.75 (3.57)	94.15 (3.27)
95% CI of LS mean	(82.34, 97.15)	(87.39, 100.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.41 (-5.79, 14.60)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	3.79 (4.66)	6.75 (4.21)
95% CI of LS mean	(-5.98, 13.56)	(-2.09, 15.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.96 (-10.40, 16.32)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	84.23 (4.07)	93.48 (3.76)
95% CI of LS mean	(75.81, 92.65)	(85.72, 101.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.25 (-2.35, 20.84)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	0.62 (5.94)	6.04 (5.47)
95% CI of LS mean	(-11.81, 13.05)	(-5.39, 17.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.42 (-11.61, 22.44)
Week 52		
n	11	13
Mean (SD)	93.94 (8.81)	93.27 (12.21)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	5.56 (12.50)	0.00 (7.08)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	93.53 (3.39)	92.52 (2.99)
95% CI of LS mean	(86.51, 100.55)	(86.30, 98.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.01 (-10.59, 8.56)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	10.14 (4.18)	3.84 (3.79)
95% CI of LS mean	(1.27, 19.02)	(-4.23, 11.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.31 (-18.51, 5.90)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	4.85 (4.58)	5.54 (4.17)
95% CI of LS mean	(-4.79, 14.50)	(-3.24, 14.32)
P-value within Treatment	0.3043	0.2010
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.69 (-12.54, 13.92)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9138
Hedges' G (SE)		0.05 (0.41)
Hedges' 95% CI		(-0.81, 0.91)
Hedges' P-value		0.9123

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	79.17 (23.44)	81.94 (15.01)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	75.62 (5.00)	84.21 (4.52)
95% CI of LS mean	(65.27, 85.97)	(74.83, 93.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.59 (-5.54, 22.72)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	-1.73 (5.67)	3.98 (4.86)
95% CI of LS mean	(-13.71, 10.25)	(-6.36, 14.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.71 (-10.30, 21.72)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	76.22 (5.79)	83.71 (5.26)
95% CI of LS mean	(64.06, 88.39)	(72.64, 94.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.49 (-9.09, 24.07)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	-5.30 (4.78)	1.63 (4.04)
95% CI of LS mean	(-15.36, 4.76)	(-6.94, 10.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.92 (-6.59, 20.43)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	77.15 (5.66)	85.72 (5.18)
95% CI of LS mean	(65.46, 88.83)	(75.06, 96.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.57 (-7.39, 24.54)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	-2.53 (5.09)	4.57 (4.75)
95% CI of LS mean	(-13.27, 8.21)	(-5.42, 14.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.10 (-7.78, 21.97)
Week 52		
n	11	13
Mean (SD)	77.78 (17.52)	79.49 (14.68)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	-8.64 (18.96)	-5.00 (11.25)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	74.29 (4.87)	80.58 (4.25)
95% CI of LS mean	(64.20, 84.39)	(71.74, 89.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.28 (-7.34, 19.90)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	-8.00 (6.48)	-2.52 (5.76)
95% CI of LS mean	(-22.21, 6.22)	(-15.26, 10.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.48 (-13.79, 24.75)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	-5.27 (4.52)	1.22 (4.04)
95% CI of LS mean	(-15.19, 4.64)	(-7.66, 10.11)
P-value within Treatment	0.2673	0.7676
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.50 (-7.10, 20.10)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3166
Hedges' G (SE)		0.44 (0.42)
Hedges' 95% CI		(-0.43, 1.31)
Hedges' P-value		0.3019

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	61.11 (30.89)	65.74 (19.80)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	69.55 (6.33)	71.37 (5.68)
95% CI of LS mean	(56.34, 82.76)	(59.49, 83.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.81 (-16.22, 19.85)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	13.30 (5.58)	4.69 (4.80)
95% CI of LS mean	(1.48, 25.11)	(-5.54, 14.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.61 (-24.40, 7.18)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	58.47 (6.73)	69.14 (6.07)
95% CI of LS mean	(44.40, 72.53)	(56.43, 81.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.68 (-8.54, 29.89)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	0.15 (6.55)	2.43 (5.77)
95% CI of LS mean	(-13.61, 13.90)	(-9.77, 14.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.29 (-16.19, 20.76)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	58.14 (7.31)	74.13 (6.75)
95% CI of LS mean	(43.01, 73.28)	(60.22, 88.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	15.99 (-4.80, 36.79)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	-2.30 (4.67)	8.95 (4.46)
95% CI of LS mean	(-12.23, 7.63)	(-0.51, 18.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.25 (-2.64, 25.15)
Week 52		
n	11	13
Mean (SD)	64.65 (22.67)	69.23 (15.15)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	-3.70 (23.57)	3.33 (15.76)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	62.27 (6.35)	69.20 (5.57)
95% CI of LS mean	(49.13, 75.41)	(57.66, 80.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.93 (-10.86, 24.73)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	-1.72 (6.78)	2.83 (6.09)
95% CI of LS mean	(-15.88, 12.43)	(-9.90, 15.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.55 (-14.59, 23.70)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	-1.29 (4.92)	4.74 (4.50)
95% CI of LS mean	(-11.68, 9.10)	(-4.77, 14.25)
P-value within Treatment	0.7958	0.3073
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.03 (-8.21, 20.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3840
Hedges' G (SE)		0.37 (0.42)
Hedges' 95% CI		(-0.49, 1.24)
Hedges' P-value		0.3807

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	72.92 (18.04)	70.00 (17.17)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	74.90 (5.08)	74.38 (4.56)
95% CI of LS mean	(64.34, 85.46)	(64.90, 83.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.52 (-14.93, 13.89)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	4.87 (5.87)	7.20 (5.26)
95% CI of LS mean	(-7.50, 17.23)	(-3.91, 18.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.33 (-14.55, 19.21)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	79.43 (5.43)	69.38 (4.90)
95% CI of LS mean	(68.19, 90.67)	(59.23, 79.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-10.05 (-25.41, 5.30)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	13.38 (6.05)	-0.36 (5.21)
95% CI of LS mean	(0.69, 26.07)	(-11.38, 10.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-13.74 (-30.82, 3.34)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	71.30 (5.83)	69.84 (5.40)
95% CI of LS mean	(59.22, 83.39)	(58.69, 80.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.47 (-18.08, 15.15)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	2.25 (6.03)	2.08 (5.59)
95% CI of LS mean	(-10.46, 14.95)	(-9.66, 13.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.16 (-17.71, 17.39)
Week 52		
n	11	13
Mean (SD)	81.21 (14.55)	74.87 (15.67)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	7.22 (17.00)	2.00 (11.78)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	80.47 (4.98)	74.73 (4.38)
95% CI of LS mean	(70.17, 90.77)	(65.63, 83.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.73 (-19.71, 8.24)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	8.40 (5.57)	4.05 (5.02)
95% CI of LS mean	(-3.39, 20.18)	(-6.59, 14.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.35 (-20.52, 11.82)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	8.01 (5.18)	1.92 (4.69)
95% CI of LS mean	(-2.90, 18.92)	(-7.97, 11.81)
P-value within Treatment	0.1401	0.6867
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.08 (-21.14, 8.97)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4059
Hedges' G (SE)		-0.36 (0.42)
Hedges' 95% CI		(-1.23, 0.51)
Hedges' P-value		0.3978

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	86.11 (22.29)	80.56 (26.43)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	75.67 (9.70)	75.82 (8.78)
95% CI of LS mean	(55.25, 96.09)	(57.37, 94.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-27.54, 27.85)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	-16.10 (10.43)	5.77 (9.29)
95% CI of LS mean	(-38.19, 5.98)	(-13.97, 25.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	21.88 (-7.98, 51.73)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	79.56 (9.20)	80.38 (8.35)
95% CI of LS mean	(59.99, 99.14)	(62.64, 98.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.82 (-25.80, 27.44)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	-14.49 (12.25)	9.08 (11.27)
95% CI of LS mean	(-40.72, 11.74)	(-15.01, 33.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	23.57 (-12.32, 59.46)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	79.46 (6.99)	92.28 (6.57)
95% CI of LS mean	(64.60, 94.31)	(78.39, 106.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	12.82 (-7.76, 33.40)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	-11.11 (9.55)	12.34 (8.83)
95% CI of LS mean	(-31.28, 9.05)	(-6.26, 30.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	23.45 (-4.29, 51.19)
Week 52		
n	11	13
Mean (SD)	90.91 (21.56)	84.62 (32.25)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	-7.41 (27.78)	16.67 (23.57)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	87.80 (8.39)	87.29 (7.36)
95% CI of LS mean	(70.50, 105.10)	(72.09, 102.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.51 (-23.80, 22.77)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	-8.62 (8.40)	12.64 (7.57)
95% CI of LS mean	(-26.22, 8.98)	(-3.24, 28.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	21.26 (-2.85, 45.37)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	-11.41 (8.95)	11.35 (8.19)
95% CI of LS mean	(-30.37, 7.55)	(-5.98, 28.68)
P-value within Treatment	0.2205	0.1843
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	22.76 (-3.29, 48.81)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0827
Hedges' G (SE)		0.77 (0.43)
Hedges' 95% CI		(-0.12, 1.67)
Hedges' P-value		0.0862

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.12.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	35	38
Mean (SD)	81.27 (17.31)	79.24 (17.70)
Week 52		
n	35	39
Mean (SD)	87.46 (15.85)	82.34 (19.41)
Absolute Change at Week 52		
n	33	36
Mean (SD)	5.39 (21.22)	3.09 (19.76)
Absolute Change at Week 52 (MMRM)		
n	31	36
LS mean (SE)	5.08 (3.85)	3.19 (3.57)
95% CI of LS mean	(-2.63, 12.79)	(-3.96, 10.33)
P-value within Treatment	0.1924	0.3757
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.89 (-12.50, 8.71)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7223

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.12.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Hedges' G (SE)		-0.09 (0.24)
Hedges' 95% CI		(-0.57, 0.40)
Hedges' P-value		0.7198

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.12.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	35	38
Mean (SD)	100.00 (0.00)	95.23 (12.11)
Week 52		
n	35	39
Mean (SD)	94.29 (14.88)	96.47 (13.05)
Absolute Change at Week 52		
n	33	36
Mean (SD)	-6.06 (15.27)	0.35 (12.50)
Absolute Change at Week 52 (MMRM)		
n	31	36
LS mean (SE)	-6.07 (2.62)	0.02 (2.43)
95% CI of LS mean	(-11.31, -0.84)	(-4.83, 4.88)
P-value within Treatment	0.0238	0.9926
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.10 (-1.11, 13.31)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0959

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.12.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Hedges' G (SE)		0.41 (0.24)
Hedges' 95% CI		(-0.08, 0.90)
Hedges' P-value		0.0959

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.12.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	35	37
Mean (SD)	82.22 (15.41)	83.03 (16.19)
Week 52		
n	35	39
Mean (SD)	85.56 (14.52)	85.04 (13.01)
Absolute Change at Week 52		
n	33	35
Mean (SD)	2.53 (15.60)	-0.16 (16.36)
Absolute Change at Week 52 (MMRM)		
n	31	35
LS mean (SE)	2.10 (3.02)	0.04 (2.83)
95% CI of LS mean	(-3.93, 8.14)	(-5.63, 5.72)
P-value within Treatment	0.4886	0.9878
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.06 (-10.41, 6.30)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6240

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.12.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Hedges' G (SE)		-0.12 (0.24)
Hedges' 95% CI		(-0.61, 0.37)
Hedges' P-value		0.6211

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.12.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	35	38
Mean (SD)	86.33 (12.66)	86.02 (15.01)
Week 52		
n	35	39
Mean (SD)	89.80 (16.19)	88.64 (12.77)
Absolute Change at Week 52		
n	33	36
Mean (SD)	3.25 (18.99)	1.67 (16.56)
Absolute Change at Week 52 (MMRM)		
n	31	36
LS mean (SE)	2.83 (3.07)	2.20 (2.84)
95% CI of LS mean	(-3.31, 8.97)	(-3.48, 7.89)
P-value within Treatment	0.3597	0.4412
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.63 (-9.08, 7.82)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8823
Hedges' G (SE)		-0.04 (0.24)

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.12.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Hedges' 95% CI		(-0.52, 0.45)
Hedges' P-value		0.8812

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.12.1.1
Study VX21-121-103: Compliance Rate for TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Baseline	35 (92.11)	38 (92.68)
Week 52	35 (92.11)	39 (95.12)
Absolute Change at Week 52	33 (86.84)	36 (87.80)

- n (%): For "Change at Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and Week 52 are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.12.1.1
Study VX21-121-103: Compliance Rate for TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Baseline	35 (92.11)	38 (92.68)
Week 52	35 (92.11)	39 (95.12)
Absolute Change at Week 52	33 (86.84)	36 (87.80)

- n (%): For "Change at Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and Week 52 are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.12.1.1
Study VX21-121-103: Compliance Rate for TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Baseline	35 (92.11)	37 (90.24)
Week 52	35 (92.11)	39 (95.12)
Absolute Change at Week 52	33 (86.84)	35 (85.37)

- n (%): For "Change at Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and Week 52 are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.12.1.1
Study VX21-121-103: Compliance Rate for TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Baseline	35 (92.11)	38 (92.68)
Week 52	35 (92.11)	39 (95.12)
Absolute Change at Week 52	33 (86.84)	36 (87.80)

- n (%): For "Change at Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and Week 52 are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.13.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	276	282
Mean (SD)	10.32 (3.43)	10.06 (3.62)
Week 4 (MMRM)		
n	273	267
LS mean (SE)	10.33 (0.22)	10.06 (0.22)
95% CI of LS mean	(9.90, 10.75)	(9.63, 10.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.27 (-0.88, 0.34)
Absolute Change at Week 4 (MMRM)		
n	261	266
LS mean (SE)	-0.03 (0.16)	-0.02 (0.16)
95% CI of LS mean	(-0.35, 0.30)	(-0.34, 0.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-0.45, 0.46)
Week 24 (MMRM)		
n	266	257
LS mean (SE)	10.55 (0.23)	10.08 (0.23)
95% CI of LS mean	(10.10, 11.00)	(9.63, 10.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-1.10, 0.17)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.13.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 24 (MMRM)		
n	254	255
LS mean (SE)	0.23 (0.18)	0.04 (0.18)
95% CI of LS mean	(-0.13, 0.59)	(-0.32, 0.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.19 (-0.69, 0.32)
Week 52		
n	273	258
Mean (SD)	10.00 (3.75)	9.58 (3.30)
Absolute Change at Week 52		
n	261	256
Mean (SD)	-0.30 (2.97)	-0.38 (2.82)
Week 52 (MMRM)		
n	264	252
LS mean (SE)	10.02 (0.21)	9.64 (0.22)
95% CI of LS mean	(9.60, 10.44)	(9.21, 10.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.39 (-0.99, 0.21)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.13.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52 (MMRM)		
n	252	250
LS mean (SE)	-0.30 (0.18)	-0.39 (0.18)
95% CI of LS mean	(-0.65, 0.06)	(-0.75, -0.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-0.60, 0.41)
Absolute Change through Week 52 (MMRM)		
n	262	262
LS mean (SE)	-0.03 (0.16)	-0.18 (0.16)
95% CI of LS mean	(-0.34, 0.27)	(-0.48, 0.13)
P-value within Treatment	0.8289	0.2599
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-0.57, 0.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5203
Hedges' G (SE)		-0.06 (0.09)
Hedges' 95% CI		(-0.23, 0.12)
Hedges' P-value		0.5201

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.13.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Physical Activity

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	277	281
Mean (SD)	12.03 (4.61)	12.00 (4.17)
Week 4 (MMRM)		
n	273	264
LS mean (SE)	12.09 (0.29)	11.96 (0.29)
95% CI of LS mean	(11.52, 12.65)	(11.39, 12.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.12 (-0.93, 0.69)
Absolute Change at Week 4 (MMRM)		
n	262	262
LS mean (SE)	0.03 (0.26)	0.00 (0.26)
95% CI of LS mean	(-0.48, 0.53)	(-0.51, 0.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-0.75, 0.69)
Week 24 (MMRM)		
n	267	259
LS mean (SE)	12.46 (0.30)	12.00 (0.30)
95% CI of LS mean	(11.87, 13.05)	(11.40, 12.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.46 (-1.30, 0.38)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.13.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Physical Activity

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 24 (MMRM)		
n	256	257
LS mean (SE)	0.37 (0.26)	0.00 (0.26)
95% CI of LS mean	(-0.14, 0.88)	(-0.51, 0.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-1.10, 0.34)
Week 52		
n	274	259
Mean (SD)	12.09 (4.89)	11.15 (3.97)
Absolute Change at Week 52		
n	263	256
Mean (SD)	0.06 (4.34)	-0.61 (3.09)
Week 52 (MMRM)		
n	265	253
LS mean (SE)	12.08 (0.27)	11.28 (0.27)
95% CI of LS mean	(11.55, 12.61)	(10.75, 11.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.80 (-1.55, -0.04)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.13.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Physical Activity

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52 (MMRM)		
n	254	250
LS mean (SE)	0.08 (0.24)	-0.63 (0.24)
95% CI of LS mean	(-0.39, 0.55)	(-1.10, -0.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.71 (-1.37, -0.04)
Absolute Change through Week 52 (MMRM)		
n	263	262
LS mean (SE)	0.22 (0.21)	-0.32 (0.21)
95% CI of LS mean	(-0.19, 0.64)	(-0.73, 0.09)
P-value within Treatment	0.2845	0.1285
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.54 (-1.13, 0.04)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0674
Hedges' G (SE)		-0.16 (0.09)
Hedges' 95% CI		(-0.33, 0.01)
Hedges' P-value		0.0676

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.13.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Social Activity

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	278	282
Mean (SD)	5.38 (2.39)	5.32 (2.06)
Week 4 (MMRM)		
n	273	266
LS mean (SE)	5.51 (0.14)	5.34 (0.14)
95% CI of LS mean	(5.23, 5.79)	(5.06, 5.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-0.57, 0.22)
Absolute Change at Week 4 (MMRM)		
n	263	265
LS mean (SE)	0.14 (0.12)	0.02 (0.12)
95% CI of LS mean	(-0.10, 0.38)	(-0.22, 0.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.12 (-0.46, 0.22)
Week 24 (MMRM)		
n	267	258
LS mean (SE)	5.49 (0.14)	5.09 (0.14)
95% CI of LS mean	(5.22, 5.77)	(4.81, 5.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.40 (-0.80, -0.01)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.13.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Social Activity

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 24 (MMRM)		
n	257	256
LS mean (SE)	0.12 (0.13)	-0.23 (0.13)
95% CI of LS mean	(-0.14, 0.37)	(-0.48, 0.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.34 (-0.70, 0.01)
Week 52		
n	274	259
Mean (SD)	5.26 (2.38)	4.94 (1.72)
Absolute Change at Week 52		
n	264	257
Mean (SD)	-0.16 (1.98)	-0.32 (1.59)
Week 52 (MMRM)		
n	265	253
LS mean (SE)	5.23 (0.13)	5.00 (0.13)
95% CI of LS mean	(4.98, 5.48)	(4.74, 5.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-0.59, 0.12)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.13.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Social Activity

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52 (MMRM)		
n	255	251
LS mean (SE)	-0.16 (0.11)	-0.30 (0.11)
95% CI of LS mean	(-0.38, 0.06)	(-0.52, -0.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-0.45, 0.17)
Absolute Change through Week 52 (MMRM)		
n	264	263
LS mean (SE)	-0.02 (0.10)	-0.26 (0.10)
95% CI of LS mean	(-0.23, 0.18)	(-0.47, -0.06)
P-value within Treatment	0.8285	0.0113
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-0.53, 0.05)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1005
Hedges' G (SE)		-0.14 (0.09)
Hedges' 95% CI		(-0.31, 0.03)
Hedges' P-value		0.1007

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.13.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Emotional

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	278	280
Mean (SD)	6.95 (2.89)	6.97 (2.82)
Week 4 (MMRM)		
n	275	269
LS mean (SE)	6.97 (0.17)	6.82 (0.17)
95% CI of LS mean	(6.64, 7.31)	(6.49, 7.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-0.62, 0.32)
Absolute Change at Week 4 (MMRM)		
n	266	267
LS mean (SE)	0.00 (0.13)	-0.19 (0.13)
95% CI of LS mean	(-0.26, 0.26)	(-0.45, 0.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.20 (-0.56, 0.17)
Week 24 (MMRM)		
n	269	260
LS mean (SE)	6.90 (0.18)	7.08 (0.18)
95% CI of LS mean	(6.55, 7.26)	(6.72, 7.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-0.33, 0.68)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.13.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Emotional

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 24 (MMRM)		
n	260	256
LS mean (SE)	-0.09 (0.16)	0.06 (0.16)
95% CI of LS mean	(-0.40, 0.23)	(-0.26, 0.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-0.30, 0.60)
Week 52		
n	274	259
Mean (SD)	6.92 (2.99)	6.78 (2.84)
Absolute Change at Week 52		
n	264	255
Mean (SD)	-0.07 (2.83)	-0.13 (2.41)
Week 52 (MMRM)		
n	265	253
LS mean (SE)	6.93 (0.18)	6.85 (0.18)
95% CI of LS mean	(6.58, 7.28)	(6.49, 7.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.58, 0.41)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.13.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Emotional

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52 (MMRM)		
n	256	249
LS mean (SE)	-0.05 (0.17)	-0.16 (0.17)
95% CI of LS mean	(-0.38, 0.28)	(-0.49, 0.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-0.58, 0.36)
Absolute Change through Week 52 (MMRM)		
n	265	261
LS mean (SE)	-0.07 (0.15)	-0.05 (0.15)
95% CI of LS mean	(-0.36, 0.22)	(-0.34, 0.24)
P-value within Treatment	0.6540	0.7532
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.02 (-0.39, 0.43)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9261
Hedges' G (SE)		0.01 (0.09)
Hedges' 95% CI		(-0.16, 0.18)
Hedges' P-value		0.9261

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.13.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Work/School Limitation

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	276	281
Mean (SD)	5.21 (2.20)	5.14 (2.07)
Week 4 (MMRM)		
n	273	265
LS mean (SE)	5.22 (0.13)	5.02 (0.13)
95% CI of LS mean	(4.97, 5.48)	(4.76, 5.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.20 (-0.56, 0.17)
Absolute Change at Week 4 (MMRM)		
n	261	263
LS mean (SE)	-0.03 (0.10)	-0.09 (0.10)
95% CI of LS mean	(-0.22, 0.17)	(-0.28, 0.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-0.34, 0.21)
Week 24 (MMRM)		
n	267	256
LS mean (SE)	5.31 (0.13)	5.05 (0.14)
95% CI of LS mean	(5.04, 5.57)	(4.78, 5.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-0.63, 0.12)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.13.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Work/School Limitation

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 24 (MMRM)		
n	255	254
LS mean (SE)	0.06 (0.11)	-0.07 (0.11)
95% CI of LS mean	(-0.15, 0.27)	(-0.28, 0.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-0.43, 0.17)
Week 52		
n	273	258
Mean (SD)	5.08 (2.28)	4.69 (1.91)
Absolute Change at Week 52		
n	261	255
Mean (SD)	-0.15 (1.77)	-0.35 (1.61)
Week 52 (MMRM)		
n	264	252
LS mean (SE)	5.06 (0.13)	4.75 (0.13)
95% CI of LS mean	(4.81, 5.31)	(4.50, 5.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-0.66, 0.05)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.13.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Work/School Limitation

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52 (MMRM)		
n	252	249
LS mean (SE)	-0.18 (0.11)	-0.35 (0.11)
95% CI of LS mean	(-0.38, 0.03)	(-0.56, -0.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-0.47, 0.12)
Absolute Change through Week 52 (MMRM)		
n	262	261
LS mean (SE)	-0.06 (0.09)	-0.21 (0.09)
95% CI of LS mean	(-0.24, 0.12)	(-0.39, -0.03)
P-value within Treatment	0.5206	0.0222
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-0.41, 0.10)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2435
Hedges' G (SE)		-0.10 (0.09)
Hedges' 95% CI		(-0.27, 0.07)
Hedges' P-value		0.2435

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.13.1.1
Study VX21-121-103: Compliance Rate for CF-IQ by Visit (All Domains)
Full Analysis Set

Domain: Control and Burden of CF Treatment

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	276 (95.50)	282 (99.30)
Week 4	283 (97.92)	273 (96.13)
Absolute Change at Week 4	271 (93.77)	272 (95.77)
Week 24	275 (95.16)	263 (92.61)
Absolute Change at Week 24	263 (91.00)	261 (91.90)
Week 52	273 (94.46)	258 (90.85)
Absolute Change at Week 52	261 (90.31)	256 (90.14)
Through Week 52	283 (97.92)	270 (95.07)
Absolute Change through Week 52	271 (93.77)	268 (94.37)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 24 and 52 can be calculated, i.e. for whom at least one of Week 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.13.1.1
Study VX21-121-103: Compliance Rate for CF-IQ by Visit (All Domains)
Full Analysis Set

Domain: Physical Activity

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	277 (95.85)	281 (98.94)
Week 4	283 (97.92)	270 (95.07)
Absolute Change at Week 4	272 (94.12)	268 (94.37)
Week 24	276 (95.50)	265 (93.31)
Absolute Change at Week 24	265 (91.70)	263 (92.61)
Week 52	274 (94.81)	259 (91.20)
Absolute Change at Week 52	263 (91.00)	256 (90.14)
Through Week 52	283 (97.92)	271 (95.42)
Absolute Change through Week 52	272 (94.12)	268 (94.37)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 24 and 52 can be calculated, i.e. for whom at least one of Week 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.13.1.1
Study VX21-121-103: Compliance Rate for CF-IQ by Visit (All Domains)
Full Analysis Set

Domain: Social Activity

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	278 (96.19)	282 (99.30)
Week 4	283 (97.92)	272 (95.77)
Absolute Change at Week 4	273 (94.46)	271 (95.42)
Week 24	276 (95.50)	264 (92.96)
Absolute Change at Week 24	266 (92.04)	262 (92.25)
Week 52	274 (94.81)	259 (91.20)
Absolute Change at Week 52	264 (91.35)	257 (90.49)
Through Week 52	283 (97.92)	271 (95.42)
Absolute Change through Week 52	273 (94.46)	269 (94.72)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 24 and 52 can be calculated, i.e. for whom at least one of Week 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.13.1.1
Study VX21-121-103: Compliance Rate for CF-IQ by Visit (All Domains)
Full Analysis Set

Domain: Emotional

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	278 (96.19)	280 (98.59)
Week 4	285 (98.62)	275 (96.83)
Absolute Change at Week 4	275 (95.16)	273 (96.13)
Week 24	278 (96.19)	266 (93.66)
Absolute Change at Week 24	268 (92.73)	262 (92.25)
Week 52	274 (94.81)	259 (91.20)
Absolute Change at Week 52	264 (91.35)	255 (89.79)
Through Week 52	283 (97.92)	271 (95.42)
Absolute Change through Week 52	273 (94.46)	267 (94.01)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 24 and 52 can be calculated, i.e. for whom at least one of Week 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.13.1.1
Study VX21-121-103: Compliance Rate for CF-IQ by Visit (All Domains)
Full Analysis Set

Domain: Work/School Limitation

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	276 (95.50)	281 (98.94)
Week 4	283 (97.92)	271 (95.42)
Absolute Change at Week 4	271 (93.77)	269 (94.72)
Week 24	276 (95.50)	262 (92.25)
Absolute Change at Week 24	264 (91.35)	260 (91.55)
Week 52	273 (94.46)	258 (90.85)
Absolute Change at Week 52	261 (90.31)	255 (89.79)
Through Week 52	283 (97.92)	270 (95.07)
Absolute Change through Week 52	271 (93.77)	267 (94.01)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 24 and 52 can be calculated, i.e. for whom at least one of Week 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.2.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ through Week 52
Full Analysis Set

Subgroup	P-value for Interaction
ppFEV$_1$ at baseline (<70 % vs. ≥70 %) [1]	0.5537
Age at screening (<18 years vs. ≥18 years) [2]	0.4366
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.4765
Sex (Male vs. Female) [1]	0.8589
Region (North America vs. Rest of the World) [1]	0.1906

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for ppFEV$_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline ppFEV$_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	167	154
mean (SD)	56.10 (9.26)	56.38 (8.74)
Week 52		
n	155	144
mean (SD)	56.26 (10.65)	56.66 (9.30)
Absolute Change at Week 52		
n	155	144
mean (SD)	0.25 (5.46)	0.41 (4.97)
Absolute Change through Week 52 (MMRM)		
n	159	149
LS mean (SE)	0.29 (0.34)	0.63 (0.35)
95% CI of LS mean	(-0.37, 0.96)	(-0.06, 1.31)
P-value within Treatment	0.3820	0.0714

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.33 (-0.62, 1.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4912
Hedges' G (SE)		0.08 (0.11)
Hedges' 95% CI		(-0.15, 0.30)
Hedges' P-value		0.4912

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	119	125
mean (SD)	80.90 (7.05)	80.60 (7.70)
Week 52		
n	114	110
mean (SD)	80.30 (8.11)	79.96 (8.27)
Absolute Change at Week 52		
n	114	110
mean (SD)	-0.53 (5.29)	-0.23 (4.75)
Absolute Change through Week 52 (MMRM)		
n	118	122
LS mean (SE)	-0.34 (0.34)	-0.15 (0.34)
95% CI of LS mean	(-1.01, 0.34)	(-0.82, 0.51)
P-value within Treatment	0.3269	0.6487

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-0.77, 1.14)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7061
Hedges' G (SE)		0.05 (0.13)
Hedges' 95% CI		(-0.20, 0.30)
Hedges' P-value		0.7052

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	38	40
mean (SD)	80.82 (10.15)	79.42 (13.73)
Week 52		
n	35	33
mean (SD)	79.75 (10.70)	78.72 (13.50)
Absolute Change at Week 52		
n	35	33
mean (SD)	-1.18 (5.94)	0.47 (7.29)
Absolute Change through Week 52 (MMRM)		
n	34	39
LS mean (SE)	-0.36 (0.80)	0.94 (0.76)
95% CI of LS mean	(-1.96, 1.23)	(-0.58, 2.46)
P-value within Treatment	0.6499	0.2204

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.30 (-0.91, 3.52)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2434
Hedges' G (SE)		0.27 (0.23)
Hedges' 95% CI		(-0.19, 0.74)
Hedges' P-value		0.2434

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	248	239
mean (SD)	64.21 (14.22)	65.20 (13.79)
Week 52		
n	236	224
mean (SD)	64.40 (14.87)	65.06 (14.25)
Absolute Change at Week 52		
n	234	221
mean (SD)	0.08 (5.30)	0.09 (4.42)
Absolute Change through Week 52 (MMRM)		
n	243	232
LS mean (SE)	0.08 (0.25)	0.21 (0.25)
95% CI of LS mean	(-0.41, 0.56)	(-0.29, 0.71)
P-value within Treatment	0.7591	0.4156

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-0.57, 0.83)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7138
Hedges' G (SE)		0.03 (0.09)
Hedges' 95% CI		(-0.15, 0.21)
Hedges' P-value		0.7136

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	79	69
mean (SD)	64.72 (14.87)	65.27 (13.99)
Week 52		
n	74	65
mean (SD)	64.55 (14.63)	65.31 (14.12)
Absolute Change at Week 52		
n	73	63
mean (SD)	-0.30 (5.34)	0.71 (5.14)
Absolute Change through Week 52 (MMRM)		
n	79	66
LS mean (SE)	-0.19 (0.44)	0.60 (0.48)
95% CI of LS mean	(-1.06, 0.67)	(-0.34, 1.55)
P-value within Treatment	0.6594	0.2096

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.80 (-0.49, 2.08)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2226
Hedges' G (SE)		0.20 (0.17)
Hedges' 95% CI		(-0.13, 0.53)
Hedges' P-value		0.2232

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	200	208
mean (SD)	67.30 (14.89)	67.91 (14.76)
Week 52		
n	191	190
mean (SD)	67.31 (15.61)	67.34 (15.07)
Absolute Change at Week 52		
n	190	189
mean (SD)	0.05 (5.47)	-0.07 (4.79)
Absolute Change through Week 52 (MMRM)		
n	198	205
LS mean (SE)	0.09 (0.29)	0.19 (0.28)
95% CI of LS mean	(-0.47, 0.66)	(-0.37, 0.74)
P-value within Treatment	0.7453	0.5048

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-0.69, 0.88)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8132
Hedges' G (SE)		0.02 (0.10)
Hedges' 95% CI		(-0.17, 0.22)
Hedges' P-value		0.8131

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	141	146
mean (SD)	67.75 (14.73)	66.55 (14.84)
Week 52		
n	135	137
mean (SD)	67.57 (15.29)	66.55 (15.09)
Absolute Change at Week 52		
n	133	134
mean (SD)	-0.35 (5.38)	0.11 (4.42)
Absolute Change through Week 52 (MMRM)		
n	134	141
LS mean (SE)	-0.15 (0.32)	0.34 (0.32)
95% CI of LS mean	(-0.79, 0.49)	(-0.29, 0.96)
P-value within Treatment	0.6527	0.2910

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.48 (-0.42, 1.38)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2919
Hedges' G (SE)		0.13 (0.12)
Hedges' 95% CI		(-0.11, 0.36)
Hedges' P-value		0.2900

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	145	133
mean (SD)	65.12 (14.91)	67.99 (14.42)
Week 52		
n	136	120
mean (SD)	65.20 (15.24)	67.12 (14.63)
Absolute Change at Week 52		
n	136	120
mean (SD)	0.17 (5.41)	0.17 (5.35)
Absolute Change through Week 52 (MMRM)		
n	143	130
LS mean (SE)	0.10 (0.36)	0.28 (0.37)
95% CI of LS mean	(-0.60, 0.80)	(-0.46, 1.01)
P-value within Treatment	0.7758	0.4618

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-0.85, 1.20)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7382
Hedges' G (SE)		0.04 (0.12)
Hedges' 95% CI		(-0.20, 0.28)
Hedges' P-value		0.7369

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	101	113
mean (SD)	68.03 (15.01)	67.07 (13.31)
Week 52		
n	97	100
mean (SD)	68.20 (15.32)	66.42 (12.29)
Absolute Change at Week 52		
n	96	100
mean (SD)	-0.28 (6.01)	0.02 (4.32)
Absolute Change through Week 52 (MMRM)		
n	99	110
LS mean (SE)	-0.40 (0.39)	0.36 (0.37)
95% CI of LS mean	(-1.17, 0.38)	(-0.38, 1.10)
P-value within Treatment	0.3169	0.3360

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.76 (-0.32, 1.83)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1660
Hedges' G (SE)		0.19 (0.14)
Hedges' 95% CI		(-0.08, 0.46)
Hedges' P-value		0.1664

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	185	166
mean (SD)	65.54 (14.73)	67.35 (15.50)
Week 52		
n	174	157
mean (SD)	65.36 (15.21)	67.07 (16.30)
Absolute Change at Week 52		
n	173	154
mean (SD)	0.02 (5.03)	0.21 (5.21)
Absolute Change through Week 52 (MMRM)		
n	178	161
LS mean (SE)	0.21 (0.30)	0.26 (0.32)
95% CI of LS mean	(-0.38, 0.81)	(-0.37, 0.88)
P-value within Treatment	0.4847	0.4159

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-0.82, 0.91)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9139
Hedges' G (SE)		0.01 (0.11)
Hedges' 95% CI		(-0.20, 0.23)
Hedges' P-value		0.9138

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.6314
Age at screening (<18 years vs. ≥18 years) [2]	0.1467
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.1661
Sex (Male vs. Female) [1]	0.1494
Region (North America vs. Rest of the World) [1]	0.3866

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

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Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	167	151
mean (SD)	23.13 (2.96)	23.69 (3.89)
Week 52		
n	157	138
mean (SD)	23.46 (3.20)	24.04 (4.27)
Absolute Change at Week 52		
n	157	135
mean (SD)	0.21 (1.13)	0.28 (1.27)
Absolute Change at Week 52 (MMRM)		
n	152	134
LS mean (SE)	0.14 (0.10)	0.27 (0.10)
95% CI of LS mean	(-0.05, 0.33)	(0.08, 0.47)
P-value within Treatment	0.1452	0.0070

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-0.14, 0.41)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3360
Hedges' G (SE)		0.11 (0.12)
Hedges' 95% CI		(-0.12, 0.35)
Hedges' P-value		0.3367

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	119	124
mean (SD)	22.64 (3.68)	22.80 (4.15)
Week 52		
n	115	116
mean (SD)	23.03 (3.79)	23.37 (4.02)
Absolute Change at Week 52		
n	115	115
mean (SD)	0.36 (1.28)	0.49 (1.29)
Absolute Change at Week 52 (MMRM)		
n	114	114
LS mean (SE)	0.32 (0.12)	0.50 (0.12)
95% CI of LS mean	(0.09, 0.55)	(0.27, 0.73)
P-value within Treatment	0.0073	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-0.15, 0.51)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2764
Hedges' G (SE)		0.14 (0.13)
Hedges' 95% CI		(-0.12, 0.40)
Hedges' P-value		0.2768

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	38	41
mean (SD)	19.68 (2.49)	20.37 (3.80)
Week 52		
n	36	36
mean (SD)	20.05 (2.25)	21.58 (4.14)
Absolute Change at Week 52		
n	36	36
mean (SD)	0.35 (1.43)	1.07 (1.10)
Absolute Change at Week 52 (MMRM)		
n	34	36
LS mean (SE)	0.24 (0.21)	1.06 (0.20)
95% CI of LS mean	(-0.18, 0.66)	(0.66, 1.47)
P-value within Treatment	0.2639	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.83 (0.25, 1.41)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0059
Hedges' G (SE)		0.67 (0.24)
Hedges' 95% CI		(0.19, 1.16)
Hedges' P-value		0.0074

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	251	239
mean (SD)	23.42 (3.09)	23.76 (3.86)
Week 52		
n	239	222
mean (SD)	23.75 (3.34)	24.07 (4.06)
Absolute Change at Week 52		
n	239	218
mean (SD)	0.25 (1.16)	0.26 (1.27)
Absolute Change at Week 52 (MMRM)		
n	232	212
LS mean (SE)	0.22 (0.08)	0.26 (0.08)
95% CI of LS mean	(0.06, 0.37)	(0.10, 0.42)
P-value within Treatment	0.0058	0.0017

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.04 (-0.18, 0.26)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7321
Hedges' G (SE)		0.03 (0.09)
Hedges' 95% CI		(-0.15, 0.22)
Hedges' P-value		0.7322

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	80	72
mean (SD)	23.45 (3.64)	23.38 (4.55)
Week 52		
n	78	67
mean (SD)	23.71 (3.91)	23.90 (4.77)
Absolute Change at Week 52		
n	78	67
mean (SD)	0.25 (1.22)	0.37 (1.05)
Absolute Change at Week 52 (MMRM)		
n	77	64
LS mean (SE)	0.24 (0.13)	0.41 (0.14)
95% CI of LS mean	(-0.02, 0.50)	(0.13, 0.69)
P-value within Treatment	0.0656	0.0044

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-0.21, 0.55)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3791
Hedges' G (SE)		0.15 (0.17)
Hedges' 95% CI		(-0.18, 0.48)
Hedges' P-value		0.3798

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	202	206
mean (SD)	22.76 (3.09)	23.21 (3.84)
Week 52		
n	191	189
mean (SD)	23.07 (3.22)	23.64 (3.93)
Absolute Change at Week 52		
n	191	185
mean (SD)	0.23 (1.15)	0.37 (1.34)
Absolute Change at Week 52 (MMRM)		
n	189	184
LS mean (SE)	0.21 (0.09)	0.36 (0.09)
95% CI of LS mean	(0.03, 0.38)	(0.18, 0.54)
P-value within Treatment	0.0214	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-0.10, 0.40)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2331
Hedges' G (SE)		0.12 (0.10)
Hedges' 95% CI		(-0.08, 0.33)
Hedges' P-value		0.2336

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	144	147
mean (SD)	23.41 (3.29)	23.53 (3.72)
Week 52		
n	139	138
mean (SD)	23.67 (3.45)	23.74 (3.79)
Absolute Change at Week 52		
n	139	136
mean (SD)	0.19 (1.16)	0.23 (1.08)
Absolute Change at Week 52 (MMRM)		
n	131	132
LS mean (SE)	0.11 (0.10)	0.23 (0.09)
95% CI of LS mean	(-0.08, 0.29)	(0.04, 0.41)
P-value within Treatment	0.2651	0.0155

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-0.14, 0.39)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3607
Hedges' G (SE)		0.11 (0.12)
Hedges' 95% CI		(-0.13, 0.36)
Hedges' P-value		0.3607

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	145	133
mean (SD)	22.44 (3.18)	22.97 (4.33)
Week 52		
n	136	120
mean (SD)	22.86 (3.40)	23.70 (4.54)
Absolute Change at Week 52		
n	136	118
mean (SD)	0.35 (1.22)	0.55 (1.46)
Absolute Change at Week 52 (MMRM)		
n	135	116
LS mean (SE)	0.33 (0.11)	0.53 (0.12)
95% CI of LS mean	(0.11, 0.55)	(0.30, 0.77)
P-value within Treatment	0.0040	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.20 (-0.12, 0.53)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2206
Hedges' G (SE)		0.15 (0.13)
Hedges' 95% CI		(-0.09, 0.40)
Hedges' P-value		0.2214

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	103	113
mean (SD)	24.05 (3.69)	24.16 (4.71)
Week 52		
n	100	104
mean (SD)	24.41 (3.96)	24.57 (4.86)
Absolute Change at Week 52		
n	100	103
mean (SD)	0.21 (1.32)	0.21 (1.27)
Absolute Change at Week 52 (MMRM)		
n	96	103
LS mean (SE)	0.18 (0.13)	0.19 (0.13)
95% CI of LS mean	(-0.08, 0.44)	(-0.06, 0.44)
P-value within Treatment	0.1726	0.1294

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-0.35, 0.37)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9487
Hedges' G (SE)		0.01 (0.14)
Hedges' 95% CI		(-0.27, 0.29)
Hedges' P-value		0.9487

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	186	167
mean (SD)	22.30 (2.83)	22.66 (3.36)
Week 52		
n	175	154
mean (SD)	22.61 (2.93)	23.15 (3.50)
Absolute Change at Week 52		
n	175	151
mean (SD)	0.30 (1.12)	0.49 (1.27)
Absolute Change at Week 52 (MMRM)		
n	170	145
LS mean (SE)	0.24 (0.09)	0.49 (0.09)
95% CI of LS mean	(0.06, 0.41)	(0.31, 0.68)
P-value within Treatment	0.0073	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.26 (0.00, 0.51)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0488
Hedges' G (SE)		0.22 (0.11)
Hedges' 95% CI		(0.00, 0.45)
Hedges' P-value		0.0497

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52
for Subjects ≤20 Years at Baseline
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.6533
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.3241
Sex (Male vs. Female) [1]	0.9032
Region (North America vs. Rest of the World) [1]	0.2317

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
Baseline		
n	8	11
mean (SD)	-0.34 (0.68)	-0.25 (1.26)
Week 52		
n	5	8
mean (SD)	-0.43 (0.94)	-0.09 (1.30)
Absolute Change at Week 52		
n	5	8
mean (SD)	0.00 (0.54)	0.03 (0.41)
Absolute Change at Week 52 (MMRM)		
n	4	8
LS mean (SE)	-0.12 (0.22)	0.01 (0.14)
95% CI of LS mean	(-0.60, 0.36)	(-0.29, 0.32)
P-value within Treatment	0.5980	0.9190

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-0.44, 0.71)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6189
Hedges' G (SE)		0.30 (0.57)
Hedges' 95% CI		(-0.96, 1.57)
Hedges' P-value		0.6045

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 34	VNZ/TEZ/D-IVA N = 41
Baseline		
n	34	41
mean (SD)	-0.29 (1.04)	-0.14 (0.88)
Week 52		
n	32	34
mean (SD)	-0.34 (1.03)	0.04 (0.88)
Absolute Change at Week 52		
n	32	34
mean (SD)	-0.10 (0.48)	0.17 (0.36)
Absolute Change at Week 52 (MMRM)		
n	31	34
LS mean (SE)	-0.14 (0.07)	0.16 (0.07)
95% CI of LS mean	(-0.28, 0.01)	(0.02, 0.30)
P-value within Treatment	0.0645	0.0230

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 34	VNZ/TEZ/D-IVA N = 41
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.30 (0.10, 0.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0043
Hedges' G (SE)		0.73 (0.25)
Hedges' 95% CI		(0.22, 1.23)
Hedges' P-value		0.0056

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 14
Baseline		
n	8	14
mean (SD)	0.02 (0.91)	-0.56 (0.97)
Week 52		
n	8	10
mean (SD)	-0.13 (0.71)	-0.33 (1.06)
Absolute Change at Week 52		
n	8	10
mean (SD)	-0.16 (0.60)	0.13 (0.55)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	-0.16 (0.19)	0.16 (0.16)
95% CI of LS mean	(-0.56, 0.24)	(-0.18, 0.51)
P-value within Treatment	0.4004	0.3352

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 14
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.33 (-0.20, 0.85)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2121
Hedges' G (SE)		0.59 (0.46)
Hedges' 95% CI		(-0.39, 1.57)
Hedges' P-value		0.2208

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 32	VNZ/TEZ/D-IVA N = 39
Baseline		
n	32	39
mean (SD)	-0.42 (1.01)	-0.03 (0.92)
Week 52		
n	27	32
mean (SD)	-0.50 (1.06)	0.13 (0.92)
Absolute Change at Week 52		
n	27	32
mean (SD)	-0.10 (0.44)	0.15 (0.31)
Absolute Change at Week 52 (MMRM)		
n	27	32
LS mean (SE)	-0.13 (0.07)	0.12 (0.06)
95% CI of LS mean	(-0.26, 0.01)	(-0.01, 0.25)
P-value within Treatment	0.0776	0.0621

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 32	VNZ/TEZ/D-IVA N = 39
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.25 (0.06, 0.43)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0116
Hedges' G (SE)		0.67 (0.27)
Hedges' 95% CI		(0.14, 1.20)
Hedges' P-value		0.0140

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 21
Baseline		
n	25	21
mean (SD)	-0.22 (1.14)	-0.23 (1.07)
Week 52		
n	21	18
mean (SD)	-0.36 (1.12)	-0.12 (1.06)
Absolute Change at Week 52		
n	21	18
mean (SD)	-0.20 (0.52)	0.10 (0.39)
Absolute Change at Week 52 (MMRM)		
n	19	18
LS mean (SE)	-0.30 (0.10)	0.05 (0.10)
95% CI of LS mean	(-0.49, -0.10)	(-0.15, 0.26)
P-value within Treatment	0.0041	0.5839

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 21
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.35 (0.07, 0.63)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0158
Hedges' G (SE)		0.82 (0.34)
Hedges' 95% CI		(0.13, 1.50)
Hedges' P-value		0.0204

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 17	VNZ/TEZ/D-IVA N = 32
Baseline		
n	17	32
mean (SD)	-0.43 (0.68)	-0.13 (0.88)
Week 52		
n	16	24
mean (SD)	-0.35 (0.87)	0.12 (0.88)
Absolute Change at Week 52		
n	16	24
mean (SD)	0.07 (0.38)	0.18 (0.36)
Absolute Change at Week 52 (MMRM)		
n	16	24
LS mean (SE)	0.05 (0.09)	0.16 (0.07)
95% CI of LS mean	(-0.13, 0.24)	(0.01, 0.30)
P-value within Treatment	0.5461	0.0337

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 17	VNZ/TEZ/D-IVA N = 32
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-0.13, 0.33)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3840
Hedges' G (SE)		0.28 (0.32)
Hedges' 95% CI		(-0.36, 0.92)
Hedges' P-value		0.3823

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 20
Baseline		
n	12	20
mean (SD)	-0.19 (1.24)	0.01 (1.06)
Week 52		
n	11	13
mean (SD)	-0.46 (1.03)	0.21 (1.33)
Absolute Change at Week 52		
n	11	13
mean (SD)	-0.31 (0.54)	-0.06 (0.35)
Absolute Change at Week 52 (MMRM)		
n	11	13
LS mean (SE)	-0.30 (0.14)	-0.09 (0.12)
95% CI of LS mean	(-0.58, -0.01)	(-0.34, 0.15)
P-value within Treatment	0.0404	0.4354

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 20
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.20 (-0.17, 0.58)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2801
Hedges' G (SE)		0.44 (0.40)
Hedges' 95% CI		(-0.39, 1.27)
Hedges' P-value		0.2812

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 30	VNZ/TEZ/D-IVA N = 33
Baseline		
n	30	33
mean (SD)	-0.35 (0.87)	-0.28 (0.88)
Week 52		
n	26	29
mean (SD)	-0.31 (1.01)	-0.07 (0.75)
Absolute Change at Week 52		
n	26	29
mean (SD)	0.01 (0.42)	0.24 (0.35)
Absolute Change at Week 52 (MMRM)		
n	24	29
LS mean (SE)	-0.02 (0.07)	0.23 (0.07)
95% CI of LS mean	(-0.17, 0.13)	(0.09, 0.36)
P-value within Treatment	0.7585	0.0014

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 30	VNZ/TEZ/D-IVA N = 33
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.25 (0.05, 0.45)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0161
Hedges' G (SE)		0.68 (0.28)
Hedges' 95% CI		(0.12, 1.24)
Hedges' P-value		0.0191

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.4.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.0895
Age at screening (<18 years vs. ≥18 years) [2]	0.6470
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.0227
Sex (Male vs. Female) [1]	0.0117
Region (North America vs. Rest of the World) [1]	0.9448

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride,genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$,genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

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Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	161	153
mean (SD)	42.26 (18.50)	42.16 (19.18)
Week 52		
n	155	138
mean (SD)	38.10 (18.34)	36.34 (20.93)
Absolute Change at Week 52		
n	153	137
mean (SD)	-3.90 (12.17)	-6.14 (14.06)
Absolute Change through Week 52 (MMRM)		
n	159	149
LS mean (SE)	-2.78 (0.81)	-4.65 (0.84)
95% CI of LS mean	(-4.38, -1.18)	(-6.31, -2.99)
P-value within Treatment	0.0007	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.87 (-4.18, 0.44)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1121
Hedges' G (SE)		-0.18 (0.11)
Hedges' 95% CI		(-0.41, 0.04)
Hedges' P-value		0.1125

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	118	124
mean (SD)	41.74 (16.77)	45.21 (17.17)
Week 52		
n	111	112
mean (SD)	42.77 (22.65)	40.99 (19.91)
Absolute Change at Week 52		
n	110	112
mean (SD)	-0.22 (17.86)	-3.85 (14.19)
Absolute Change through Week 52 (MMRM)		
n	118	122
LS mean (SE)	-1.45 (1.02)	-5.30 (1.01)
95% CI of LS mean	(-3.46, 0.57)	(-7.29, -3.32)
P-value within Treatment	0.1578	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.85 (-6.69, -1.02)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0079
Hedges' G (SE)		-0.35 (0.13)
Hedges' 95% CI		(-0.60, -0.09)
Hedges' P-value		0.0082

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	36	41
mean (SD)	45.85 (18.39)	43.68 (17.58)
Week 52		
n	35	36
mean (SD)	47.30 (26.94)	40.75 (19.79)
Absolute Change at Week 52		
n	34	36
mean (SD)	0.43 (21.14)	-1.62 (12.31)
Absolute Change through Week 52 (MMRM)		
n	34	39
LS mean (SE)	0.40 (2.15)	-2.54 (2.04)
95% CI of LS mean	(-3.91, 4.70)	(-6.63, 1.55)
P-value within Treatment	0.8541	0.2190

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.94 (-8.91, 3.04)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3289
Hedges' G (SE)		-0.23 (0.23)
Hedges' 95% CI		(-0.69, 0.23)
Hedges' P-value		0.3275

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	246	241
mean (SD)	41.52 (17.78)	43.39 (18.73)
Week 52		
n	234	218
mean (SD)	38.98 (19.08)	37.73 (20.72)
Absolute Change at Week 52		
n	232	217
mean (SD)	-2.79 (13.66)	-5.68 (14.24)
Absolute Change through Week 52 (MMRM)		
n	243	232
LS mean (SE)	-2.54 (0.66)	-5.24 (0.68)
95% CI of LS mean	(-3.83, -1.24)	(-6.57, -3.91)
P-value within Treatment	0.0001	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.70 (-4.56, -0.84)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0045
Hedges' G (SE)		-0.26 (0.09)
Hedges' 95% CI		(-0.44, -0.08)
Hedges' P-value		0.0046

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	80	72
mean (SD)	21.39 (5.38)	21.20 (5.86)
Week 52		
n	74	63
mean (SD)	22.41 (8.73)	19.29 (9.06)
Absolute Change at Week 52		
n	74	63
mean (SD)	0.96 (7.77)	-1.61 (7.77)
Absolute Change through Week 52 (MMRM)		
n	79	67
LS mean (SE)	1.04 (0.86)	0.00 (0.93)
95% CI of LS mean	(-0.66, 2.74)	(-1.85, 1.86)
P-value within Treatment	0.2269	0.9970

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.04 (-3.56, 1.48)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4154
Hedges' G (SE)		-0.14 (0.17)
Hedges' 95% CI		(-0.46, 0.19)
Hedges' P-value		0.4141

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	202	210
mean (SD)	50.27 (14.07)	51.05 (14.89)
Week 52		
n	192	190
mean (SD)	46.57 (19.33)	44.57 (19.39)
Absolute Change at Week 52		
n	192	190
mean (SD)	-3.67 (16.60)	-6.26 (15.40)
Absolute Change through Week 52 (MMRM)		
n	198	204
LS mean (SE)	-3.39 (0.82)	-6.68 (0.81)
95% CI of LS mean	(-5.00, -1.77)	(-8.28, -5.09)
P-value within Treatment	<0.0001	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.29 (-5.56, -1.03)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0046
Hedges' G (SE)		-0.28 (0.10)
Hedges' 95% CI		(-0.48, -0.09)
Hedges' P-value		0.0047

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	139	148
mean (SD)	43.95 (17.37)	45.90 (17.62)
Week 52		
n	135	136
mean (SD)	43.28 (22.51)	39.73 (19.01)
Absolute Change at Week 52		
n	133	135
mean (SD)	-1.01 (17.72)	-6.57 (13.02)
Absolute Change through Week 52 (MMRM)		
n	134	142
LS mean (SE)	-1.35 (0.90)	-6.54 (0.87)
95% CI of LS mean	(-3.11, 0.42)	(-8.27, -4.82)
P-value within Treatment	0.1347	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.20 (-7.68, -2.72)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-0.50 (0.12)
Hedges' 95% CI		(-0.74, -0.26)
Hedges' P-value		<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	143	134
mean (SD)	40.25 (18.24)	40.70 (19.20)
Week 52		
n	134	118
mean (SD)	36.82 (17.53)	36.36 (22.20)
Absolute Change at Week 52		
n	133	118
mean (SD)	-3.75 (11.08)	-3.42 (14.98)
Absolute Change through Week 52 (MMRM)		
n	143	129
LS mean (SE)	-3.01 (0.91)	-3.27 (0.96)
95% CI of LS mean	(-4.80, -1.23)	(-5.17, -1.38)
P-value within Treatment	0.0010	0.0008

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-2.87, 2.35)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8448
Hedges' G (SE)		-0.02 (0.12)
Hedges' 95% CI		(-0.26, 0.21)
Hedges' P-value		0.8442

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	101	114
mean (SD)	43.35 (17.11)	44.25 (17.10)
Week 52		
n	97	100
mean (SD)	43.32 (22.54)	40.35 (18.80)
Absolute Change at Week 52		
n	96	100
mean (SD)	0.09 (16.96)	-3.93 (13.60)
Absolute Change through Week 52 (MMRM)		
n	99	110
LS mean (SE)	0.18 (1.08)	-3.03 (1.03)
95% CI of LS mean	(-1.95, 2.32)	(-5.05, -1.00)
P-value within Treatment	0.8665	0.0037

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.21 (-6.16, -0.26)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0332
Hedges' G (SE)		-0.30 (0.14)
Hedges' 95% CI		(-0.57, -0.02)
Hedges' P-value		0.0338

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	181	168
mean (SD)	41.36 (18.31)	42.88 (19.49)
Week 52		
n	172	154
mean (SD)	38.22 (18.92)	36.74 (21.61)
Absolute Change at Week 52		
n	170	153
mean (SD)	-3.77 (13.30)	-5.87 (14.29)
Absolute Change through Week 52 (MMRM)		
n	178	161
LS mean (SE)	-3.65 (0.75)	-6.15 (0.79)
95% CI of LS mean	(-5.12, -2.18)	(-7.71, -4.60)
P-value within Treatment	<0.0001	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.50 (-4.64, -0.36)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0223
Hedges' G (SE)		-0.25 (0.11)
Hedges' 95% CI		(-0.46, -0.04)
Hedges' P-value		0.0226

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.4.2.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1076*
Age at screening (<18 years vs. ≥18 years) [2]	0.4326*
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.6086*
Sex (Male vs. Female) [1]	0.1505*
Region (North America vs. Rest of the World) [1]	0.4406*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at Baseline <70%

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Non-missing value at Week 52, N1	155	138
Number of subjects with missing value at Week 52	12	16
SwCl <60 mmol/L at Week 52, n (%)	139 (83.23)	121 (78.57)
Relative Risk (RR) (95% CI)		0.9180 (0.8316, 1.0135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0902*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at Baseline ≥70%

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Non-missing value at Week 52, N1	111	112
Number of subjects with missing value at Week 52	8	13
SwCl <60 mmol/L at Week 52, n (%)	93 (78.15)	98 (78.40)
Relative Risk (RR) (95% CI)		1.0548 (0.9461, 1.1760)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3364

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years),and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

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Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Age at Screening < 18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Non-missing value at Week 52, N1	35	36
Number of subjects with missing value at Week 52	3	5
SwCl <60 mmol/L at Week 52, n (%)	27 (71.05)	32 (78.05)
Relative Risk (RR) (95% CI)		1.0466 (0.8449, 1.2964)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6768*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Age at Screening ≥ 18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Non-missing value at Week 52, N1	234	218
Number of subjects with missing value at Week 52	17	25
SwCl <60 mmol/L at Week 52, n (%)	207 (82.47)	191 (78.60)
Relative Risk (RR) (95% CI)		0.9556 (0.8796, 1.0382)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2831*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Non-missing value at Week 52, N1	74	63
Number of subjects with missing value at Week 52	6	9
SwCl <60 mmol/L at Week 52, n (%)	74 (92.50)	63 (87.50)
Relative Risk (RR) (95% CI)		0.9399 (0.8419, 1.0494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2704*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Non-missing value at Week 52, N1	192	190
Number of subjects with missing value at Week 52	10	20
SwCl <60 mmol/L at Week 52, n (%)	158 (78.22)	159 (75.71)
Relative Risk (RR) (95% CI)		0.9776 (0.8864, 1.0782)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6502*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Non-missing value at Week 52, N1	135	136
Number of subjects with missing value at Week 52	9	13
SwCl <60 mmol/L at Week 52, n (%)	111 (77.08)	120 (80.54)
Relative Risk (RR) (95% CI)		1.0156 (0.9020, 1.1436)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7980

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years),and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Non-missing value at Week 52, N1	134	118
Number of subjects with missing value at Week 52	11	17
SwCl <60 mmol/L at Week 52, n (%)	123 (84.83)	103 (76.30)
Relative Risk (RR) (95% CI)		0.9176 (0.8239, 1.0220)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1177*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Non-missing value at Week 52, N1	97	100
Number of subjects with missing value at Week 52	6	14
SwCl <60 mmol/L at Week 52, n (%)	80 (77.67)	89 (78.07)
Relative Risk (RR) (95% CI)		1.0132 (0.8866, 1.1578)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.8475*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Non-missing value at Week 52, N1	172	154
Number of subjects with missing value at Week 52	14	16
SwCl <60 mmol/L at Week 52, n (%)	154 (82.80)	134 (78.82)
Relative Risk (RR) (95% CI)		0.9460 (0.8601, 1.0404)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2528*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline $ppFEV_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.9805*
Age at screening (<18 years vs. ≥18 years) [2]	0.2502*
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.2430*
Sex (Male vs. Female) [1]	0.4742*
Region (North America vs. Rest of the World) [1]	0.8645*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at Baseline <70%

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Non-missing value at Week 52, N1	155	138
Number of subjects with missing value at Week 52	12	16
SwCl <30 mmol/L at Week 52, n (%)	55 (32.93)	62 (40.26)
Relative Risk (RR) (95% CI)		1.1089 (0.8756, 1.4044)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3911*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at Baseline ≥70%

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Non-missing value at Week 52, N1	111	112
Number of subjects with missing value at Week 52	8	13
SwCl <30 mmol/L at Week 52, n (%)	37 (31.09)	35 (28.00)
Relative Risk (RR) (95% CI)		1.1134 (0.8133, 1.5244)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.5026*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Age at Screening < 18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Non-missing value at Week 52, N1	35	36
Number of subjects with missing value at Week 52	3	5
SwCl <30 mmol/L at Week 52, n (%)	11 (28.95)	11 (26.83)
Relative Risk (RR) (95% CI)		0.7228 (0.3696, 1.4135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3428*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline $ppFEV_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

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Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Age at Screening ≥ 18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Non-missing value at Week 52, N1	234	218
Number of subjects with missing value at Week 52	17	25
SwCl <30 mmol/L at Week 52, n (%)	82 (32.67)	89 (36.63)
Relative Risk (RR) (95% CI)		1.1520 (0.9428, 1.4077)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1664*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Non-missing value at Week 52, N1	74	63
Number of subjects with missing value at Week 52	6	9
SwCl <30 mmol/L at Week 52, n (%)	61 (76.25)	57 (79.17)
Relative Risk (RR) (95% CI)		1.0236 (0.8633, 1.2136)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7887*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Non-missing value at Week 52, N1	192	190
Number of subjects with missing value at Week 52	10	20
SwCl <30 mmol/L at Week 52, n (%)	32 (15.84)	42 (20.00)
Relative Risk (RR) (95% CI)		1.3275 (0.9116, 1.9332)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1396*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Non-missing value at Week 52, N1	135	136
Number of subjects with missing value at Week 52	9	13
SwCl <30 mmol/L at Week 52, n (%)	39 (27.08)	47 (31.54)
Relative Risk (RR) (95% CI)		1.1734 (0.8563, 1.6080)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3199*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Non-missing value at Week 52, N1	134	118
Number of subjects with missing value at Week 52	11	17
SwCl <30 mmol/L at Week 52, n (%)	54 (37.24)	53 (39.26)
Relative Risk (RR) (95% CI)		1.0219 (0.8078, 1.2926)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.8569*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Non-missing value at Week 52, N1	97	100
Number of subjects with missing value at Week 52	6	14
SwCl <30 mmol/L at Week 52, n (%)	28 (27.18)	33 (28.95)
Relative Risk (RR) (95% CI)		1.1699 (0.8123, 1.6849)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3993*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Non-missing value at Week 52, N1	172	154
Number of subjects with missing value at Week 52	14	16
SwCl <30 mmol/L at Week 52, n (%)	65 (34.95)	67 (39.41)
Relative Risk (RR) (95% CI)		1.1250 (0.8998, 1.4064)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3013*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline $ppFEV_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.5.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.5752
Age at screening (<18 years vs. ≥18 years) [2]	0.2218
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.1729
Sex (Male vs. Female) [1]	0.2002
Region (North America vs. Rest of the World) [1]	0.2801

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

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Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	167	151
mean (SD)	65.49 (12.13)	68.06 (12.76)
Week 52		
n	157	138
mean (SD)	66.64 (12.30)	68.94 (13.35)
Absolute Change at Week 52		
n	157	135
mean (SD)	0.60 (3.20)	0.75 (3.38)
Absolute Change at Week 52 (MMRM)		
n	152	134
LS mean (SE)	0.38 (0.26)	0.75 (0.27)
95% CI of LS mean	(-0.13, 0.89)	(0.21, 1.28)
P-value within Treatment	0.1401	0.0064

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-0.37, 1.10)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3310
Hedges' G (SE)		0.12 (0.12)
Hedges' 95% CI		(-0.12, 0.35)
Hedges' P-value		0.3317

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	119	124
mean (SD)	64.33 (14.89)	64.90 (15.05)
Week 52		
n	115	116
mean (SD)	66.04 (14.44)	67.14 (14.74)
Absolute Change at Week 52		
n	115	115
mean (SD)	1.53 (3.88)	2.02 (4.41)
Absolute Change at Week 52 (MMRM)		
n	114	114
LS mean (SE)	1.38 (0.38)	2.02 (0.37)
95% CI of LS mean	(0.64, 2.13)	(1.28, 2.75)
P-value within Treatment	0.0003	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-0.41, 1.68)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2343
Hedges' G (SE)		0.16 (0.13)
Hedges' 95% CI		(-0.10, 0.42)
Hedges' P-value		0.2349

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	38	41
mean (SD)	52.50 (9.78)	54.20 (11.96)
Week 52		
n	36	36
mean (SD)	55.32 (8.73)	59.35 (13.26)
Absolute Change at Week 52		
n	36	36
mean (SD)	2.93 (4.39)	4.94 (4.03)
Absolute Change at Week 52 (MMRM)		
n	34	36
LS mean (SE)	2.54 (0.70)	4.87 (0.67)
95% CI of LS mean	(1.14, 3.93)	(3.53, 6.22)
P-value within Treatment	0.0005	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.33 (0.40, 4.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0188
Hedges' G (SE)		0.57 (0.24)
Hedges' 95% CI		(0.09, 1.05)
Hedges' P-value		0.0212

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	251	239
mean (SD)	66.95 (12.79)	68.70 (13.20)
Week 52		
n	239	222
mean (SD)	68.07 (12.98)	69.58 (13.63)
Absolute Change at Week 52		
n	239	218
mean (SD)	0.68 (3.28)	0.73 (3.57)
Absolute Change at Week 52 (MMRM)		
n	232	212
LS mean (SE)	0.57 (0.22)	0.72 (0.23)
95% CI of LS mean	(0.14, 1.00)	(0.27, 1.17)
P-value within Treatment	0.0099	0.0017

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-0.47, 0.77)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6389
Hedges' G (SE)		0.04 (0.09)
Hedges' 95% CI		(-0.14, 0.23)
Hedges' P-value		0.6390

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	80	72
mean (SD)	66.01 (13.23)	66.56 (15.17)
Week 52		
n	78	67
mean (SD)	67.12 (13.76)	68.03 (15.47)
Absolute Change at Week 52		
n	78	67
mean (SD)	0.80 (3.41)	1.12 (3.09)
Absolute Change at Week 52 (MMRM)		
n	77	64
LS mean (SE)	0.79 (0.37)	1.23 (0.40)
95% CI of LS mean	(0.06, 1.52)	(0.43, 2.02)
P-value within Treatment	0.0337	0.0029

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-0.65, 1.52)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4304
Hedges' G (SE)		0.13 (0.17)
Hedges' 95% CI		(-0.20, 0.47)
Hedges' P-value		0.4309

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	202	206
mean (SD)	64.79 (13.40)	66.51 (13.57)
Week 52		
n	191	189
mean (SD)	65.99 (12.97)	68.08 (13.51)
Absolute Change at Week 52		
n	191	185
mean (SD)	0.87 (3.40)	1.38 (4.17)
Absolute Change at Week 52 (MMRM)		
n	189	184
LS mean (SE)	0.82 (0.27)	1.34 (0.27)
95% CI of LS mean	(0.29, 1.35)	(0.80, 1.87)
P-value within Treatment	0.0027	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.52 (-0.24, 1.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1785
Hedges' G (SE)		0.14 (0.10)
Hedges' 95% CI		(-0.06, 0.34)
Hedges' P-value		0.1791

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	144	147
mean (SD)	71.57 (13.16)	71.42 (13.53)
Week 52		
n	139	138
mean (SD)	72.79 (12.86)	72.52 (13.65)
Absolute Change at Week 52		
n	139	136
mean (SD)	0.91 (3.71)	1.15 (3.88)
Absolute Change at Week 52 (MMRM)		
n	131	132
LS mean (SE)	0.63 (0.32)	1.16 (0.32)
95% CI of LS mean	(0.00, 1.26)	(0.54, 1.79)
P-value within Treatment	0.0511	0.0003

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.53 (-0.35, 1.42)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2375
Hedges' G (SE)		0.15 (0.12)
Hedges' 95% CI		(-0.10, 0.39)
Hedges' P-value		0.2378

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	145	133
mean (SD)	58.57 (9.96)	61.23 (12.47)
Week 52		
n	136	120
mean (SD)	59.88 (10.03)	63.13 (12.72)
Absolute Change at Week 52		
n	136	118
mean (SD)	1.03 (3.32)	1.53 (3.95)
Absolute Change at Week 52 (MMRM)		
n	135	116
LS mean (SE)	0.99 (0.31)	1.49 (0.33)
95% CI of LS mean	(0.39, 1.60)	(0.85, 2.13)
P-value within Treatment	0.0014	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-0.39, 1.38)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2679
Hedges' G (SE)		0.14 (0.13)
Hedges' 95% CI		(-0.11, 0.39)
Hedges' P-value		0.2687

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	103	113
mean (SD)	67.86 (14.29)	68.77 (15.46)
Week 52		
n	100	104
mean (SD)	69.25 (14.85)	70.47 (15.30)
Absolute Change at Week 52		
n	100	103
mean (SD)	0.91 (3.86)	0.75 (3.80)
Absolute Change at Week 52 (MMRM)		
n	96	103
LS mean (SE)	0.83 (0.39)	0.70 (0.37)
95% CI of LS mean	(0.06, 1.59)	(-0.04, 1.43)
P-value within Treatment	0.0338	0.0627

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-1.19, 0.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8034
Hedges' G (SE)		-0.04 (0.14)
Hedges' 95% CI		(-0.31, 0.24)
Hedges' P-value		0.8034

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	186	167
mean (SD)	63.49 (12.56)	65.10 (12.72)
Week 52		
n	175	154
mean (SD)	64.78 (11.93)	66.58 (12.89)
Absolute Change at Week 52		
n	175	151
mean (SD)	1.01 (3.32)	1.72 (3.95)
Absolute Change at Week 52 (MMRM)		
n	170	145
LS mean (SE)	0.80 (0.27)	1.73 (0.28)
95% CI of LS mean	(0.28, 1.33)	(1.18, 2.29)
P-value within Treatment	0.0026	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (0.17, 1.69)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0173
Hedges' G (SE)		0.27 (0.11)
Hedges' 95% CI		(0.05, 0.49)
Hedges' P-value		0.0179

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.6.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Time-to-First Pulmonary Exacerbation through Week 52
Full Analysis Set

Subgroup	P-value for Interaction based on Hazard Ratio
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.3664
Age at screening (<18 years vs. ≥18 years) [2]	0.5177
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.4264
Sex (Male vs. Female) [1]	0.7052
Region (North America vs. Rest of the World) [1]	0.9381

-Subgroup Criteria (SC): subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
-P-values are reported for each subgroup factor only when SC are fulfilled. If not, display '-'.
- [1] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$ and baseline sweat chloride,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- [2] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$,(F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride.
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Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at Baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	41 (24.55)	36 (23.38)
Subjects Censored	126 (75.45)	118 (76.62)
Event-free time (weeks)		
75 percent subjects	51.4286	52.5714
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9940 (0.9583, 0.9992)	1.0000 (-, -)
4 Weeks	0.9760 (0.9374, 0.9909)	0.9935 (0.9548, 0.9991)
8 Weeks	0.9519 (0.9062, 0.9757)	0.9803 (0.9403, 0.9936)
12 Weeks	0.9218 (0.8692, 0.9538)	0.9407 (0.8891, 0.9687)
16 Weeks	0.8915 (0.8333, 0.9302)	0.9007 (0.8406, 0.9389)
24 Weeks	0.8485 (0.7841, 0.8950)	0.8398 (0.7705, 0.8896)
36 Weeks	0.8051 (0.7358, 0.8580)	0.7991 (0.7254, 0.8550)
52 Weeks	0.7486 (0.6744, 0.8082)	0.7650 (0.6883, 0.8253)
Hazard Ratio (95% CI)*	-	0.9453 (0.6010, 1.4867)
Two-sided P-value, superiority*	-	0.8076

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at Baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	18 (15.13)	24 (19.20)
Subjects Censored	101 (84.87)	101 (80.80)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9664 (0.9129, 0.9872)	0.9760 (0.9274, 0.9922)
4 Weeks	0.9580 (0.9020, 0.9823)	0.9600 (0.9066, 0.9832)
8 Weeks	0.9412 (0.8806, 0.9715)	0.9440 (0.8861, 0.9729)
12 Weeks	0.9328 (0.8701, 0.9658)	0.9038 (0.8368, 0.9442)
16 Weeks	0.9328 (0.8701, 0.9658)	0.8956 (0.8271, 0.9380)
24 Weeks	0.9244 (0.8597, 0.9599)	0.8793 (0.8078, 0.9254)
36 Weeks	0.8908 (0.8193, 0.9351)	0.8374 (0.7593, 0.8919)
52 Weeks	0.8451 (0.7649, 0.8997)	0.8035 (0.7211, 0.8638)
Hazard Ratio (95% CI)*	-	1.2934 (0.6985, 2.3952)
Two-sided P-value, superiority*	-	0.4131

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	4 (10.53)	8 (19.51)
Subjects Censored	34 (89.47)	33 (80.49)
Event-free time (weeks)		
75 percent subjects	-	52.5714
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9512 (0.8187, 0.9876)
4 Weeks	1.0000 (-, -)	0.9512 (0.8187, 0.9876)
8 Weeks	1.0000 (-, -)	0.9512 (0.8187, 0.9876)
12 Weeks	1.0000 (-, -)	0.9512 (0.8187, 0.9876)
16 Weeks	0.9730 (0.8232, 0.9961)	0.9018 (0.7591, 0.9620)
24 Weeks	0.9452 (0.7980, 0.9860)	0.9018 (0.7591, 0.9620)
36 Weeks	0.9174 (0.7652, 0.9726)	0.8745 (0.7238, 0.9458)
52 Weeks	0.8868 (0.7253, 0.9560)	0.8198 (0.6580, 0.9100)
Hazard Ratio (95% CI)*	-	1.6933 (0.4743, 6.0448)
Two-sided P-value, superiority*	-	0.4173

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	55 (21.91)	53 (21.81)
Subjects Censored	196 (78.09)	190 (78.19)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9801 (0.9528, 0.9917)	0.9959 (0.9711, 0.9994)
4 Weeks	0.9641 (0.9322, 0.9812)	0.9835 (0.9567, 0.9938)
8 Weeks	0.9402 (0.9028, 0.9635)	0.9669 (0.9350, 0.9833)
12 Weeks	0.9163 (0.8746, 0.9446)	0.9210 (0.8790, 0.9489)
16 Weeks	0.9003 (0.8561, 0.9315)	0.8958 (0.8497, 0.9284)
24 Weeks	0.8722 (0.8242, 0.9079)	0.8491 (0.7971, 0.8888)
36 Weeks	0.8318 (0.7793, 0.8728)	0.8067 (0.7505, 0.8515)
52 Weeks	0.7775 (0.7201, 0.8245)	0.7766 (0.7180, 0.8245)
Hazard Ratio (95% CI)*	-	1.0374 (0.7089, 1.5183)
Two-sided P-value, superiority*	-	0.8500

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	21 (26.25)	15 (20.83)
Subjects Censored	59 (73.75)	57 (79.17)
Event-free time (weeks)		
75 percent subjects	51.4286	52.5714
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9875 (0.9146, 0.9982)	1.0000 (-, -)
8 Weeks	0.9625 (0.8882, 0.9877)	1.0000 (-, -)
12 Weeks	0.9375 (0.8563, 0.9735)	0.9859 (0.9042, 0.9980)
16 Weeks	0.9125 (0.8252, 0.9573)	0.9432 (0.8558, 0.9783)
24 Weeks	0.8875 (0.7950, 0.9398)	0.8990 (0.7997, 0.9506)
36 Weeks	0.8246 (0.7219, 0.8922)	0.8543 (0.7460, 0.9189)
52 Weeks	0.7320 (0.6185, 0.8166)	0.7944 (0.6774, 0.8728)
Hazard Ratio (95% CI)*	-	0.8727 (0.4469, 1.7043)
Two-sided P-value, superiority*	-	0.6901

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	37 (18.32)	46 (21.90)
Subjects Censored	165 (81.68)	164 (78.10)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9752 (0.9416, 0.9896)	0.9857 (0.9564, 0.9954)
4 Weeks	0.9604 (0.9224, 0.9800)	0.9714 (0.9375, 0.9871)
8 Weeks	0.9405 (0.8976, 0.9658)	0.9523 (0.9131, 0.9740)
12 Weeks	0.9206 (0.8736, 0.9506)	0.9041 (0.8554, 0.9371)
16 Weeks	0.9056 (0.8560, 0.9387)	0.8799 (0.8274, 0.9172)
24 Weeks	0.8754 (0.8211, 0.9140)	0.8408 (0.7834, 0.8841)
36 Weeks	0.8501 (0.7926, 0.8927)	0.8015 (0.7403, 0.8498)
52 Weeks	0.8142 (0.7529, 0.8618)	0.7766 (0.7133, 0.8277)
Hazard Ratio (95% CI)*	-	1.1967 (0.7732, 1.8523)
Two-sided P-value, superiority*	-	0.4204

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	23 (15.97)	25 (16.78)
Subjects Censored	121 (84.03)	124 (83.22)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9861 (0.9456, 0.9965)	0.9866 (0.9474, 0.9966)
4 Weeks	0.9792 (0.9368, 0.9932)	0.9732 (0.9301, 0.9898)
8 Weeks	0.9512 (0.9003, 0.9764)	0.9664 (0.9212, 0.9859)
12 Weeks	0.9232 (0.8656, 0.9567)	0.9459 (0.8948, 0.9726)
16 Weeks	0.9232 (0.8656, 0.9567)	0.9321 (0.8775, 0.9629)
24 Weeks	0.9162 (0.8571, 0.9515)	0.9113 (0.8520, 0.9475)
36 Weeks	0.8878 (0.8233, 0.9297)	0.8765 (0.8111, 0.9203)
52 Weeks	0.8375 (0.7655, 0.8889)	0.8347 (0.7636, 0.8861)
Hazard Ratio (95% CI)*	-	1.0445 (0.5832, 1.8707)
Two-sided P-value, superiority*	-	0.8836

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	36 (24.83)	36 (26.67)
Subjects Censored	109 (75.17)	99 (73.33)
Event-free time (weeks)		
75 percent subjects	52.0000	37.5714
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9793 (0.9372, 0.9933)	0.9926 (0.9486, 0.9990)
4 Weeks	0.9586 (0.9102, 0.9812)	0.9852 (0.9421, 0.9963)
8 Weeks	0.9448 (0.8927, 0.9720)	0.9628 (0.9129, 0.9843)
12 Weeks	0.9310 (0.8756, 0.9623)	0.9031 (0.8390, 0.9425)
16 Weeks	0.8963 (0.8339, 0.9361)	0.8581 (0.7866, 0.9071)
24 Weeks	0.8475 (0.7777, 0.8968)	0.7969 (0.7179, 0.8560)
36 Weeks	0.7984 (0.7230, 0.8553)	0.7503 (0.6671, 0.8155)
52 Weeks	0.7457 (0.6648, 0.8098)	0.7263 (0.6412, 0.7944)
Hazard Ratio (95% CI)*	-	1.1903 (0.7420, 1.9092)
Two-sided P-value, superiority*	-	0.4700

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	21 (20.39)	26 (22.81)
Subjects Censored	82 (79.61)	88 (77.19)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9612 (0.8998, 0.9852)	1.0000 (-, -)
4 Weeks	0.9417 (0.8749, 0.9734)	0.9912 (0.9394, 0.9988)
8 Weeks	0.9223 (0.8507, 0.9604)	0.9735 (0.9202, 0.9914)
12 Weeks	0.9126 (0.8388, 0.9535)	0.9558 (0.8971, 0.9814)
16 Weeks	0.9028 (0.8269, 0.9465)	0.9200 (0.8519, 0.9576)
24 Weeks	0.9028 (0.8269, 0.9465)	0.8654 (0.7866, 0.9166)
36 Weeks	0.8537 (0.7692, 0.9091)	0.8196 (0.7344, 0.8797)
52 Weeks	0.7949 (0.7029, 0.8611)	0.7639 (0.6729, 0.8327)
Hazard Ratio (95% CI)*	-	1.0432 (0.5812, 1.8723)
Two-sided P-value, superiority*	-	0.8874

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	38 (20.43)	35 (20.59)
Subjects Censored	148 (79.57)	135 (79.41)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9946 (0.9625, 0.9992)	0.9824 (0.9463, 0.9943)
4 Weeks	0.9839 (0.9508, 0.9948)	0.9706 (0.9308, 0.9877)
8 Weeks	0.9622 (0.9224, 0.9818)	0.9588 (0.9154, 0.9801)
12 Weeks	0.9352 (0.8887, 0.9627)	0.9052 (0.8500, 0.9408)
16 Weeks	0.9136 (0.8628, 0.9462)	0.8812 (0.8220, 0.9217)
24 Weeks	0.8699 (0.8122, 0.9109)	0.8509 (0.7874, 0.8967)
36 Weeks	0.8368 (0.7750, 0.8830)	0.8143 (0.7464, 0.8656)
52 Weeks	0.7900 (0.7228, 0.8428)	0.7957 (0.7260, 0.8495)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Hazard Ratio (95% CI)*	-	1.0859 (0.6831, 1.7260)
Two-sided P-value, superiority*	-	0.7275

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Time-to-First Pulmonary Exacerbation Requiring Hospitalizatio through Week 52
Full Analysis Set

Subgroup	P-value for Interaction based on Hazard Ratio
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.3882
Age at screening (<18 years vs. ≥18 years) [2]	0.2962
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.1969
Sex (Male vs. Female) [1]	0.5194
Region (North America vs. Rest of the World) [1]	0.4918

- Subgroup Criteria (SC): subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when SC are fulfilled. If not, display '-'.
- [1] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$ and baseline sweat chloride,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- [2] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$,(F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

ppFEV$_1$ at Baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	6 (3.59)	6 (3.90)
Subjects Censored	161 (96.41)	148 (96.10)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	0.9935 (0.9548, 0.9991)
8 Weeks	1.0000 (-, -)	0.9935 (0.9548, 0.9991)
12 Weeks	0.9940 (0.9580, 0.9991)	0.9935 (0.9548, 0.9991)
16 Weeks	0.9940 (0.9580, 0.9991)	0.9935 (0.9548, 0.9991)
24 Weeks	0.9755 (0.9361, 0.9907)	0.9800 (0.9392, 0.9935)
36 Weeks	0.9755 (0.9361, 0.9907)	0.9597 (0.9125, 0.9817)
52 Weeks	0.9629 (0.9194, 0.9832)	0.9597 (0.9125, 0.9817)
Hazard Ratio (95% CI)*	-	1.0039 (0.3213, 3.1364)
Two-sided P-value, superiority*	-	0.9946

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

ppFEV$_1$ at Baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	3 (2.52)	7 (5.60)
Subjects Censored	116 (97.48)	118 (94.40)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9920 (0.9446, 0.9989)
4 Weeks	0.9916 (0.9419, 0.9988)	0.9920 (0.9446, 0.9989)
8 Weeks	0.9916 (0.9419, 0.9988)	0.9920 (0.9446, 0.9989)
12 Weeks	0.9916 (0.9419, 0.9988)	0.9920 (0.9446, 0.9989)
16 Weeks	0.9916 (0.9419, 0.9988)	0.9839 (0.9370, 0.9959)
24 Weeks	0.9916 (0.9419, 0.9988)	0.9757 (0.9265, 0.9921)
36 Weeks	0.9748 (0.9239, 0.9918)	0.9507 (0.8934, 0.9775)
52 Weeks	0.9748 (0.9239, 0.9918)	0.9421 (0.8823, 0.9720)
Hazard Ratio (95% CI)*	-	2.1496 (0.5502, 8.3978)
Two-sided P-value, superiority*	-	0.2710

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	1 (2.63)	5 (12.20)
Subjects Censored	37 (97.37)	36 (87.80)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9756 (0.8392, 0.9965)
4 Weeks	1.0000 (-, -)	0.9756 (0.8392, 0.9965)
8 Weeks	1.0000 (-, -)	0.9756 (0.8392, 0.9965)
12 Weeks	1.0000 (-, -)	0.9756 (0.8392, 0.9965)
16 Weeks	1.0000 (-, -)	0.9262 (0.7883, 0.9756)
24 Weeks	0.9722 (0.8187, 0.9960)	0.9262 (0.7883, 0.9756)
36 Weeks	0.9722 (0.8187, 0.9960)	0.8989 (0.7523, 0.9609)
52 Weeks	0.9722 (0.8187, 0.9960)	0.8717 (0.7182, 0.9446)
Hazard Ratio (95% CI)*	-	13.4580 (0.7881, 229.8245)
Two-sided P-value, superiority*	-	0.0726

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	8 (3.19)	9 (3.70)
Subjects Censored	243 (96.81)	234 (96.30)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9960 (0.9721, 0.9994)	0.9959 (0.9711, 0.9994)
8 Weeks	0.9960 (0.9721, 0.9994)	0.9959 (0.9711, 0.9994)
12 Weeks	0.9920 (0.9685, 0.9980)	0.9959 (0.9711, 0.9994)
16 Weeks	0.9920 (0.9685, 0.9980)	0.9959 (0.9711, 0.9994)
24 Weeks	0.9840 (0.9578, 0.9940)	0.9832 (0.9558, 0.9937)
36 Weeks	0.9759 (0.9471, 0.9891)	0.9620 (0.9282, 0.9800)
52 Weeks	0.9677 (0.9364, 0.9837)	0.9620 (0.9282, 0.9800)
Hazard Ratio (95% CI)*	-	1.1516 (0.4431, 2.9925)
Two-sided P-value, superiority*	-	0.7721

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	4 (5.00)	2 (2.78)
Subjects Censored	76 (95.00)	70 (97.22)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9875 (0.9146, 0.9982)	1.0000 (-, -)
8 Weeks	0.9875 (0.9146, 0.9982)	1.0000 (-, -)
12 Weeks	0.9875 (0.9146, 0.9982)	1.0000 (-, -)
16 Weeks	0.9875 (0.9146, 0.9982)	1.0000 (-, -)
24 Weeks	0.9625 (0.8882, 0.9877)	1.0000 (-, -)
36 Weeks	0.9625 (0.8882, 0.9877)	0.9704 (0.8867, 0.9925)
52 Weeks	0.9497 (0.8714, 0.9808)	0.9704 (0.8867, 0.9925)
Hazard Ratio (95% CI)*	-	0.5144 (0.0900, 2.9397)
Two-sided P-value, superiority*	-	0.4548

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	5 (2.48)	12 (5.71)
Subjects Censored	197 (97.52)	198 (94.29)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9952 (0.9667, 0.9993)
4 Weeks	1.0000 (-, -)	0.9905 (0.9625, 0.9976)
8 Weeks	1.0000 (-, -)	0.9905 (0.9625, 0.9976)
12 Weeks	0.9950 (0.9652, 0.9993)	0.9905 (0.9625, 0.9976)
16 Weeks	0.9950 (0.9652, 0.9993)	0.9808 (0.9496, 0.9927)
24 Weeks	0.9900 (0.9606, 0.9975)	0.9662 (0.9303, 0.9837)
36 Weeks	0.9799 (0.9473, 0.9924)	0.9465 (0.9055, 0.9700)
52 Weeks	0.9748 (0.9406, 0.9894)	0.9415 (0.8993, 0.9664)
Hazard Ratio (95% CI)*	-	2.1398 (0.7423, 6.1685)
Two-sided P-value, superiority*	-	0.1590

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	2 (1.39)	5 (3.36)
Subjects Censored	142 (98.61)	144 (96.64)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9933 (0.9533, 0.9991)
4 Weeks	1.0000 (-, -)	0.9866 (0.9474, 0.9966)
8 Weeks	1.0000 (-, -)	0.9866 (0.9474, 0.9966)
12 Weeks	0.9930 (0.9514, 0.9990)	0.9866 (0.9474, 0.9966)
16 Weeks	0.9930 (0.9514, 0.9990)	0.9866 (0.9474, 0.9966)
24 Weeks	0.9930 (0.9514, 0.9990)	0.9866 (0.9474, 0.9966)
36 Weeks	0.9930 (0.9514, 0.9990)	0.9727 (0.9288, 0.9897)
52 Weeks	0.9858 (0.9442, 0.9964)	0.9657 (0.9196, 0.9856)
Hazard Ratio (95% CI)*	-	2.3632 (0.4520, 12.3556)
Two-sided P-value, superiority*	-	0.3082

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	7 (4.83)	9 (6.67)
Subjects Censored	138 (95.17)	126 (93.33)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9931 (0.9521, 0.9990)	1.0000 (-, -)
8 Weeks	0.9931 (0.9521, 0.9990)	1.0000 (-, -)
12 Weeks	0.9931 (0.9521, 0.9990)	1.0000 (-, -)
16 Weeks	0.9931 (0.9521, 0.9990)	0.9850 (0.9414, 0.9962)
24 Weeks	0.9722 (0.9276, 0.9895)	0.9621 (0.9114, 0.9841)
36 Weeks	0.9582 (0.9093, 0.9810)	0.9312 (0.8719, 0.9636)
52 Weeks	0.9511 (0.9002, 0.9764)	0.9312 (0.8719, 0.9636)
Hazard Ratio (95% CI)*	-	1.2198 (0.4374, 3.4020)
Two-sided P-value, superiority*	-	0.7041

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	3 (2.91)	8 (7.02)
Subjects Censored	100 (97.09)	106 (92.98)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	1.0000 (-, -)
12 Weeks	1.0000 (-, -)	1.0000 (-, -)
16 Weeks	1.0000 (-, -)	0.9821 (0.9302, 0.9955)
24 Weeks	1.0000 (-, -)	0.9548 (0.8948, 0.9809)
36 Weeks	0.9804 (0.9239, 0.9951)	0.9364 (0.8712, 0.9692)
52 Weeks	0.9705 (0.9113, 0.9904)	0.9271 (0.8596, 0.9629)
Hazard Ratio (95% CI)*	-	2.1660 (0.5519, 8.5007)
Two-sided P-value, superiority*	-	0.2679

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	6 (3.23)	6 (3.53)
Subjects Censored	180 (96.77)	164 (96.47)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9941 (0.9590, 0.9992)
4 Weeks	0.9946 (0.9625, 0.9992)	0.9882 (0.9538, 0.9970)
8 Weeks	0.9946 (0.9625, 0.9992)	0.9882 (0.9538, 0.9970)
12 Weeks	0.9892 (0.9576, 0.9973)	0.9882 (0.9538, 0.9970)
16 Weeks	0.9892 (0.9576, 0.9973)	0.9882 (0.9538, 0.9970)
24 Weeks	0.9728 (0.9359, 0.9886)	0.9882 (0.9538, 0.9970)
36 Weeks	0.9728 (0.9359, 0.9886)	0.9639 (0.9213, 0.9836)
52 Weeks	0.9672 (0.9285, 0.9851)	0.9639 (0.9213, 0.9836)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Hazard Ratio (95% CI)*	-	1.1096 (0.3577, 3.4427)
Two-sided P-value, superiority*	-	0.8571

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Subgroup	P-value for Interaction based on Hazard Ratio
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1668
Age at screening (<18 years vs. ≥18 years) [2]	0.2029
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.7654
Sex (Male vs. Female) [1]	0.8345
Region (North America vs. Rest of the World) [1]	0.2591

- Subgroup Criteria (SC): subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when SC are fulfilled. If not, display '-'.
- [1] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$ and baseline sweat chloride,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- [2] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$,(F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

ppFEV$_1$ at Baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	13 (7.78)	9 (5.84)
Subjects Censored	154 (92.22)	145 (94.16)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9940 (0.9583, 0.9992)	0.9935 (0.9548, 0.9991)
8 Weeks	0.9880 (0.9528, 0.9970)	0.9869 (0.9487, 0.9967)
12 Weeks	0.9759 (0.9372, 0.9909)	0.9869 (0.9487, 0.9967)
16 Weeks	0.9759 (0.9372, 0.9909)	0.9869 (0.9487, 0.9967)
24 Weeks	0.9452 (0.8973, 0.9711)	0.9600 (0.9131, 0.9818)
36 Weeks	0.9329 (0.8820, 0.9622)	0.9397 (0.8873, 0.9682)
52 Weeks	0.9202 (0.8666, 0.9529)	0.9397 (0.8873, 0.9682)
Hazard Ratio (95% CI)*	-	0.7584 (0.3187, 1.8044)
Two-sided P-value, superiority*	-	0.5317

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

ppFEV$_1$ at Baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	4 (3.36)	9 (7.20)
Subjects Censored	115 (96.64)	116 (92.80)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9920 (0.9446, 0.9989)
4 Weeks	0.9916 (0.9419, 0.9988)	0.9920 (0.9446, 0.9989)
8 Weeks	0.9916 (0.9419, 0.9988)	0.9920 (0.9446, 0.9989)
12 Weeks	0.9832 (0.9345, 0.9958)	0.9839 (0.9373, 0.9960)
16 Weeks	0.9832 (0.9345, 0.9958)	0.9758 (0.9269, 0.9921)
24 Weeks	0.9832 (0.9345, 0.9958)	0.9676 (0.9160, 0.9877)
36 Weeks	0.9748 (0.9239, 0.9918)	0.9426 (0.8833, 0.9722)
52 Weeks	0.9664 (0.9129, 0.9872)	0.9256 (0.8618, 0.9606)
Hazard Ratio (95% CI)*	-	2.0885 (0.6364, 6.8540)
Two-sided P-value, superiority*	-	0.2245

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	1 (2.63)	5 (12.20)
Subjects Censored	37 (97.37)	36 (87.80)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9756 (0.8392, 0.9965)
4 Weeks	1.0000 (-, -)	0.9756 (0.8392, 0.9965)
8 Weeks	1.0000 (-, -)	0.9756 (0.8392, 0.9965)
12 Weeks	1.0000 (-, -)	0.9756 (0.8392, 0.9965)
16 Weeks	1.0000 (-, -)	0.9262 (0.7883, 0.9756)
24 Weeks	0.9722 (0.8187, 0.9960)	0.9262 (0.7883, 0.9756)
36 Weeks	0.9722 (0.8187, 0.9960)	0.8989 (0.7523, 0.9609)
52 Weeks	0.9722 (0.8187, 0.9960)	0.8717 (0.7182, 0.9446)
Hazard Ratio (95% CI)*	-	13.4580 (0.7881, 229.8245)
Two-sided P-value, superiority*	-	0.0726

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	16 (6.37)	14 (5.76)
Subjects Censored	235 (93.63)	229 (94.24)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9920 (0.9685, 0.9980)	0.9959 (0.9711, 0.9994)
8 Weeks	0.9880 (0.9634, 0.9961)	0.9917 (0.9674, 0.9979)
12 Weeks	0.9761 (0.9476, 0.9892)	0.9876 (0.9619, 0.9960)
16 Weeks	0.9761 (0.9476, 0.9892)	0.9876 (0.9619, 0.9960)
24 Weeks	0.9600 (0.9269, 0.9783)	0.9664 (0.9339, 0.9831)
36 Weeks	0.9479 (0.9119, 0.9694)	0.9452 (0.9075, 0.9678)
52 Weeks	0.9356 (0.8971, 0.9601)	0.9409 (0.9023, 0.9646)
Hazard Ratio (95% CI)*	-	0.9219 (0.4433, 1.9169)
Two-sided P-value, superiority*	-	0.8276

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	4 (5.00)	3 (4.17)
Subjects Censored	76 (95.00)	69 (95.83)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9875 (0.9146, 0.9982)	1.0000 (-, -)
8 Weeks	0.9875 (0.9146, 0.9982)	1.0000 (-, -)
12 Weeks	0.9875 (0.9146, 0.9982)	1.0000 (-, -)
16 Weeks	0.9875 (0.9146, 0.9982)	1.0000 (-, -)
24 Weeks	0.9625 (0.8882, 0.9877)	0.9855 (0.9016, 0.9979)
36 Weeks	0.9625 (0.8882, 0.9877)	0.9559 (0.8693, 0.9856)
52 Weeks	0.9497 (0.8714, 0.9808)	0.9559 (0.8693, 0.9856)
Hazard Ratio (95% CI)*	-	0.8429 (0.1775, 4.0019)
Two-sided P-value, superiority*	-	0.8297

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	12 (5.94)	16 (7.62)
Subjects Censored	190 (94.06)	194 (92.38)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9952 (0.9667, 0.9993)
4 Weeks	0.9950 (0.9654, 0.9993)	0.9905 (0.9625, 0.9976)
8 Weeks	0.9901 (0.9609, 0.9975)	0.9857 (0.9563, 0.9954)
12 Weeks	0.9751 (0.9413, 0.9896)	0.9809 (0.9498, 0.9928)
16 Weeks	0.9751 (0.9413, 0.9896)	0.9712 (0.9370, 0.9869)
24 Weeks	0.9600 (0.9217, 0.9798)	0.9517 (0.9120, 0.9737)
36 Weeks	0.9499 (0.9089, 0.9727)	0.9320 (0.8879, 0.9592)
52 Weeks	0.9398 (0.8964, 0.9654)	0.9221 (0.8759, 0.9515)
Hazard Ratio (95% CI)*	-	1.1670 (0.5450, 2.4990)
Two-sided P-value, superiority*	-	0.6909

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	5 (3.47)	5 (3.36)
Subjects Censored	139 (96.53)	144 (96.64)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9933 (0.9533, 0.9991)
4 Weeks	1.0000 (-, -)	0.9866 (0.9474, 0.9966)
8 Weeks	0.9930 (0.9514, 0.9990)	0.9866 (0.9474, 0.9966)
12 Weeks	0.9860 (0.9452, 0.9965)	0.9866 (0.9474, 0.9966)
16 Weeks	0.9860 (0.9452, 0.9965)	0.9866 (0.9474, 0.9966)
24 Weeks	0.9860 (0.9452, 0.9965)	0.9866 (0.9474, 0.9966)
36 Weeks	0.9789 (0.9361, 0.9932)	0.9727 (0.9288, 0.9897)
52 Weeks	0.9646 (0.9170, 0.9851)	0.9657 (0.9196, 0.9856)
Hazard Ratio (95% CI)*	-	1.0971 (0.2900, 4.1506)
Two-sided P-value, superiority*	-	0.8914

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	12 (8.28)	14 (10.37)
Subjects Censored	133 (91.72)	121 (89.63)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9862 (0.9460, 0.9965)	1.0000 (-, -)
8 Weeks	0.9862 (0.9460, 0.9965)	0.9925 (0.9482, 0.9989)
12 Weeks	0.9724 (0.9282, 0.9896)	0.9851 (0.9416, 0.9962)
16 Weeks	0.9724 (0.9282, 0.9896)	0.9701 (0.9223, 0.9887)
24 Weeks	0.9375 (0.8834, 0.9670)	0.9320 (0.8733, 0.9640)
36 Weeks	0.9235 (0.8662, 0.9569)	0.9010 (0.8356, 0.9413)
52 Weeks	0.9165 (0.8576, 0.9517)	0.8932 (0.8263, 0.9353)
Hazard Ratio (95% CI)*	-	1.2211 (0.5520, 2.7015)
Two-sided P-value, superiority*	-	0.6219

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	4 (3.88)	10 (8.77)
Subjects Censored	99 (96.12)	104 (91.23)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9903 (0.9331, 0.9986)	1.0000 (-, -)
8 Weeks	0.9903 (0.9331, 0.9986)	1.0000 (-, -)
12 Weeks	0.9806 (0.9246, 0.9951)	1.0000 (-, -)
16 Weeks	0.9806 (0.9246, 0.9951)	0.9821 (0.9302, 0.9955)
24 Weeks	0.9806 (0.9246, 0.9951)	0.9457 (0.8831, 0.9752)
36 Weeks	0.9708 (0.9121, 0.9905)	0.9273 (0.8599, 0.9630)
52 Weeks	0.9609 (0.8991, 0.9851)	0.9089 (0.8372, 0.9499)
Hazard Ratio (95% CI)*	-	1.9655 (0.5995, 6.4444)
Two-sided P-value, superiority*	-	0.2647

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	13 (6.99)	9 (5.29)
Subjects Censored	173 (93.01)	161 (94.71)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9941 (0.9590, 0.9992)
4 Weeks	0.9946 (0.9625, 0.9992)	0.9882 (0.9538, 0.9970)
8 Weeks	0.9892 (0.9576, 0.9973)	0.9823 (0.9462, 0.9943)
12 Weeks	0.9784 (0.9435, 0.9918)	0.9764 (0.9383, 0.9911)
16 Weeks	0.9784 (0.9435, 0.9918)	0.9764 (0.9383, 0.9911)
24 Weeks	0.9510 (0.9080, 0.9742)	0.9704 (0.9303, 0.9876)
36 Weeks	0.9400 (0.8944, 0.9663)	0.9460 (0.8988, 0.9715)
52 Weeks	0.9290 (0.8808, 0.9581)	0.9460 (0.8988, 0.9715)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Hazard Ratio (95% CI)*	-	0.8210 (0.3448, 1.9545)
Two-sided P-value, superiority*	-	0.6558

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.9.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.0580
Age at screening (<18 years vs. ≥18 years) [2]	0.1215
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.9161
Sex (Male vs. Female) [1]	0.7890
Region (North America vs. Rest of the World) [1]	0.2167

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	164	152
Mean (SD)	83.63 (12.75)	84.21 (14.14)
Week 8 (MMRM)		
n	161	153
LS mean (SE)	81.61 (1.36)	82.80 (1.39)
95% CI of LS mean	(78.94, 84.27)	(80.06, 85.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.19 (-2.63, 5.01)
Absolute Change at Week 8 (MMRM)		
n	158	151
LS mean (SE)	-1.96 (1.33)	-1.36 (1.36)
95% CI of LS mean	(-4.59, 0.67)	(-4.04, 1.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.60 (-3.15, 4.36)
Week 16 (MMRM)		
n	157	149
LS mean (SE)	81.54 (1.40)	83.96 (1.43)
95% CI of LS mean	(78.79, 84.29)	(81.14, 86.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.42 (-1.52, 6.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 16 (MMRM)		
n	154	147
LS mean (SE)	-1.92 (1.35)	-0.12 (1.38)
95% CI of LS mean	(-4.57, 0.72)	(-2.83, 2.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.80 (-1.99, 5.59)
Week 24 (MMRM)		
n	156	147
LS mean (SE)	79.65 (1.30)	82.67 (1.34)
95% CI of LS mean	(77.09, 82.21)	(80.03, 85.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.02 (-0.66, 6.70)
Absolute Change at Week 24 (MMRM)		
n	153	145
LS mean (SE)	-3.87 (1.18)	-1.23 (1.21)
95% CI of LS mean	(-6.18, -1.55)	(-3.61, 1.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.63 (-0.69, 5.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52		
n	159	144
Mean (SD)	81.80 (17.88)	85.22 (13.79)
Absolute Change at Week 52		
n	156	142
Mean (SD)	-1.45 (17.14)	1.36 (13.82)
Week 52 (MMRM)		
n	155	143
LS mean (SE)	81.82 (1.26)	84.96 (1.31)
95% CI of LS mean	(79.34, 84.31)	(82.38, 87.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.13 (-0.45, 6.72)
Absolute Change at Week 52 (MMRM)		
n	152	141
LS mean (SE)	-1.65 (1.28)	1.05 (1.32)
95% CI of LS mean	(-4.16, 0.86)	(-1.55, 3.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.70 (-0.92, 6.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-rd-ag12-52wks-sub-103.sas Creation: 13JAN2025 11:57

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	-2.48 (0.95)	-0.10 (0.98)
95% CI of LS mean	(-4.36, -0.60)	(-2.03, 1.83)
P-value within Treatment	0.0098	0.9179
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-0.32, 5.07)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0833
Hedges' G (SE)		0.20 (0.11)
Hedges' 95% CI		(-0.03, 0.42)
Hedges' P-value		0.0837

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	115	123
Mean (SD)	88.33 (13.47)	87.89 (11.66)
Week 8 (MMRM)		
n	116	121
LS mean (SE)	89.95 (1.25)	87.00 (1.22)
95% CI of LS mean	(87.49, 92.41)	(84.59, 89.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.95 (-6.40, 0.49)
Absolute Change at Week 8 (MMRM)		
n	112	120
LS mean (SE)	1.33 (1.46)	-0.97 (1.41)
95% CI of LS mean	(-1.53, 4.20)	(-3.75, 1.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.31 (-6.31, 1.69)
Week 16 (MMRM)		
n	115	119
LS mean (SE)	90.29 (1.26)	86.70 (1.24)
95% CI of LS mean	(87.80, 92.77)	(84.26, 89.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.59 (-7.08, -0.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 16 (MMRM)		
n	111	118
LS mean (SE)	1.66 (1.35)	-1.24 (1.31)
95% CI of LS mean	(-1.00, 4.33)	(-3.82, 1.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.91 (-6.63, 0.81)
Week 24 (MMRM)		
n	118	118
LS mean (SE)	89.11 (1.30)	85.06 (1.29)
95% CI of LS mean	(86.55, 91.66)	(82.52, 87.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.04 (-7.65, -0.44)
Absolute Change at Week 24 (MMRM)		
n	114	117
LS mean (SE)	0.57 (1.43)	-2.61 (1.40)
95% CI of LS mean	(-2.24, 3.39)	(-5.37, 0.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.18 (-7.14, 0.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52		
n	115	116
Mean (SD)	89.13 (14.70)	89.70 (11.91)
Absolute Change at Week 52		
n	111	114
Mean (SD)	0.28 (17.65)	1.60 (12.86)
Week 52 (MMRM)		
n	114	115
LS mean (SE)	89.28 (1.24)	89.61 (1.23)
95% CI of LS mean	(86.84, 91.71)	(87.19, 92.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.34 (-3.10, 3.78)
Absolute Change at Week 52 (MMRM)		
n	110	113
LS mean (SE)	0.52 (1.47)	1.61 (1.44)
95% CI of LS mean	(-2.38, 3.42)	(-1.23, 4.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.09 (-2.97, 5.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change through Week 52 (MMRM)		
n	114	120
LS mean (SE)	0.92 (1.17)	-0.75 (1.14)
95% CI of LS mean	(-1.38, 3.22)	(-2.99, 1.50)
P-value within Treatment	0.4313	0.5127
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.67 (-4.89, 1.55)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3093
Hedges' G (SE)		-0.13 (0.13)
Hedges' 95% CI		(-0.39, 0.12)
Hedges' P-value		0.3083

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	37	40
Mean (SD)	87.76 (16.41)	89.97 (11.92)
Week 8 (MMRM)		
n	34	37
LS mean (SE)	92.73 (1.83)	91.92 (1.75)
95% CI of LS mean	(89.09, 96.38)	(88.42, 95.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.81 (-5.90, 4.27)
Absolute Change at Week 8 (MMRM)		
n	33	37
LS mean (SE)	5.30 (2.73)	1.45 (2.58)
95% CI of LS mean	(-0.14, 10.75)	(-3.70, 6.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.86 (-11.40, 3.68)
Week 16 (MMRM)		
n	32	36
LS mean (SE)	91.75 (2.12)	87.78 (2.02)
95% CI of LS mean	(87.51, 96.00)	(83.75, 91.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.97 (-9.85, 1.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 16 (MMRM)		
n	31	36
LS mean (SE)	3.83 (2.48)	-2.58 (2.33)
95% CI of LS mean	(-1.12, 8.78)	(-7.24, 2.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.41 (-13.27, 0.45)
Week 24 (MMRM)		
n	34	36
LS mean (SE)	87.79 (2.29)	88.51 (2.22)
95% CI of LS mean	(83.21, 92.37)	(84.08, 92.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.72 (-5.67, 7.11)
Absolute Change at Week 24 (MMRM)		
n	33	35
LS mean (SE)	-0.58 (3.02)	-1.51 (2.90)
95% CI of LS mean	(-6.61, 5.45)	(-7.29, 4.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.92 (-9.31, 7.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52		
n	33	34
Mean (SD)	93.27 (9.45)	93.06 (8.98)
Absolute Change at Week 52		
n	32	33
Mean (SD)	4.60 (17.61)	0.25 (11.23)
Week 52 (MMRM)		
n	32	34
LS mean (SE)	93.76 (1.69)	92.64 (1.65)
95% CI of LS mean	(90.37, 97.15)	(89.34, 95.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.12 (-5.87, 3.63)
Absolute Change at Week 52 (MMRM)		
n	31	33
LS mean (SE)	4.84 (2.70)	1.62 (2.60)
95% CI of LS mean	(-0.58, 10.25)	(-3.57, 6.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.21 (-10.75, 4.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change through Week 52 (MMRM)		
n	33	38
LS mean (SE)	2.69 (2.31)	-0.82 (2.20)
95% CI of LS mean	(-1.92, 7.31)	(-5.21, 3.57)
P-value within Treatment	0.2477	0.7101
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.52 (-9.94, 2.91)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2784
Hedges' G (SE)		-0.26 (0.24)
Hedges' 95% CI		(-0.73, 0.21)
Hedges' P-value		0.2770

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	85.30 (12.66)	85.00 (13.27)
Week 8 (MMRM)		
n	243	237
LS mean (SE)	84.00 (1.04)	83.52 (1.06)
95% CI of LS mean	(81.95, 86.05)	(81.44, 85.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.48 (-3.40, 2.44)
Absolute Change at Week 8 (MMRM)		
n	237	234
LS mean (SE)	-1.44 (1.05)	-1.60 (1.06)
95% CI of LS mean	(-3.51, 0.62)	(-3.68, 0.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-3.09, 2.78)
Week 16 (MMRM)		
n	240	232
LS mean (SE)	84.21 (1.06)	84.74 (1.08)
95% CI of LS mean	(82.13, 86.29)	(82.63, 86.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.53 (-2.43, 3.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 16 (MMRM)		
n	234	229
LS mean (SE)	-1.10 (1.03)	-0.28 (1.04)
95% CI of LS mean	(-3.12, 0.92)	(-2.32, 1.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.82 (-2.05, 3.69)
Week 24 (MMRM)		
n	240	229
LS mean (SE)	83.02 (1.01)	82.95 (1.03)
95% CI of LS mean	(81.03, 85.01)	(80.92, 84.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-2.92, 2.77)
Absolute Change at Week 24 (MMRM)		
n	234	227
LS mean (SE)	-2.28 (0.95)	-1.92 (0.96)
95% CI of LS mean	(-4.14, -0.41)	(-3.82, -0.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.35 (-2.31, 3.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52		
n	244	230
Mean (SD)	83.74 (17.40)	86.38 (13.47)
Absolute Change at Week 52		
n	238	227
Mean (SD)	-1.51 (17.16)	1.74 (13.71)
Week 52 (MMRM)		
n	237	224
LS mean (SE)	83.72 (0.99)	86.12 (1.02)
95% CI of LS mean	(81.77, 85.67)	(84.12, 88.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.40 (-0.40, 5.19)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	-1.60 (1.03)	1.34 (1.05)
95% CI of LS mean	(-3.62, 0.42)	(-0.72, 3.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.94 (0.05, 5.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	-1.66 (0.77)	-0.29 (0.78)
95% CI of LS mean	(-3.17, -0.14)	(-1.83, 1.25)
P-value within Treatment	0.0324	0.7152
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.37 (-0.79, 3.54)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2140
Hedges' G (SE)		0.12 (0.09)
Hedges' 95% CI		(-0.07, 0.30)
Hedges' P-value		0.2137

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	78	71
Mean (SD)	84.15 (14.64)	87.03 (12.24)
Week 8 (MMRM)		
n	79	69
LS mean (SE)	85.58 (1.79)	85.03 (1.91)
95% CI of LS mean	(82.05, 89.11)	(81.25, 88.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.55 (-5.74, 4.63)
Absolute Change at Week 8 (MMRM)		
n	77	68
LS mean (SE)	1.31 (2.04)	-2.04 (2.17)
95% CI of LS mean	(-2.72, 5.34)	(-6.33, 2.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.35 (-9.25, 2.55)
Week 16 (MMRM)		
n	76	67
LS mean (SE)	81.99 (2.04)	84.79 (2.18)
95% CI of LS mean	(77.95, 86.03)	(80.48, 89.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.80 (-3.11, 8.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 16 (MMRM)		
n	74	66
LS mean (SE)	-2.07 (2.02)	-2.14 (2.15)
95% CI of LS mean	(-6.08, 1.93)	(-6.39, 2.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-5.92, 5.78)
Week 24 (MMRM)		
n	79	63
LS mean (SE)	79.71 (1.91)	83.65 (2.13)
95% CI of LS mean	(75.92, 83.49)	(79.44, 87.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.94 (-1.72, 9.61)
Absolute Change at Week 24 (MMRM)		
n	77	63
LS mean (SE)	-4.43 (1.88)	-2.90 (2.06)
95% CI of LS mean	(-8.14, -0.71)	(-6.98, 1.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.52 (-4.01, 7.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52		
n	78	66
Mean (SD)	82.30 (17.74)	87.96 (13.49)
Absolute Change at Week 52		
n	76	65
Mean (SD)	-1.90 (18.85)	1.84 (13.59)
Week 52 (MMRM)		
n	77	63
LS mean (SE)	82.74 (1.76)	88.09 (1.94)
95% CI of LS mean	(79.27, 86.22)	(84.25, 91.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.35 (0.17, 10.54)
Absolute Change at Week 52 (MMRM)		
n	75	62
LS mean (SE)	-1.51 (1.93)	1.77 (2.12)
95% CI of LS mean	(-5.33, 2.31)	(-2.42, 5.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.28 (-2.41, 8.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change through Week 52 (MMRM)		
n	77	66
LS mean (SE)	-2.67 (1.46)	-1.09 (1.58)
95% CI of LS mean	(-5.56, 0.22)	(-4.22, 2.03)
P-value within Treatment	0.0704	0.4912
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.58 (-2.70, 5.85)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4672
Hedges' G (SE)		0.12 (0.17)
Hedges' 95% CI		(-0.21, 0.45)
Hedges' P-value		0.4658

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	197	207
Mean (SD)	86.25 (12.52)	85.28 (13.51)
Week 8 (MMRM)		
n	198	205
LS mean (SE)	84.98 (1.11)	84.54 (1.09)
95% CI of LS mean	(82.79, 87.17)	(82.39, 86.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.44 (-3.51, 2.63)
Absolute Change at Week 8 (MMRM)		
n	193	203
LS mean (SE)	-1.32 (1.13)	-0.91 (1.10)
95% CI of LS mean	(-3.54, 0.90)	(-3.07, 1.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.41 (-2.69, 3.50)
Week 16 (MMRM)		
n	196	201
LS mean (SE)	86.53 (1.09)	85.29 (1.08)
95% CI of LS mean	(84.39, 88.68)	(83.17, 87.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.25 (-4.26, 1.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 16 (MMRM)		
n	191	199
LS mean (SE)	0.24 (1.09)	-0.16 (1.07)
95% CI of LS mean	(-1.90, 2.38)	(-2.25, 1.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.40 (-3.39, 2.60)
Week 24 (MMRM)		
n	195	202
LS mean (SE)	85.25 (1.04)	83.80 (1.03)
95% CI of LS mean	(83.20, 87.31)	(81.78, 85.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.46 (-4.33, 1.42)
Absolute Change at Week 24 (MMRM)		
n	190	199
LS mean (SE)	-1.01 (1.03)	-1.54 (1.01)
95% CI of LS mean	(-3.04, 1.03)	(-3.53, 0.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.54 (-3.38, 2.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52		
n	194	196
Mean (SD)	85.81 (16.61)	87.04 (13.02)
Absolute Change at Week 52		
n	189	193
Mean (SD)	-0.44 (16.81)	1.47 (13.44)
Week 52 (MMRM)		
n	192	195
LS mean (SE)	85.81 (1.03)	86.73 (1.02)
95% CI of LS mean	(83.78, 87.83)	(84.72, 88.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.92 (-1.93, 3.77)
Absolute Change at Week 52 (MMRM)		
n	187	192
LS mean (SE)	-0.45 (1.11)	1.18 (1.09)
95% CI of LS mean	(-2.63, 1.73)	(-0.96, 3.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.63 (-1.43, 4.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-rd-ag12-52wks-sub-103.sas Creation: 13JAN2025 11:57

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change through Week 52 (MMRM)		
n	193	202
LS mean (SE)	-0.41 (0.86)	-0.18 (0.84)
95% CI of LS mean	(-2.09, 1.28)	(-1.82, 1.47)
P-value within Treatment	0.6347	0.8339
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.23 (-2.13, 2.59)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8471
Hedges' G (SE)		0.02 (0.10)
Hedges' 95% CI		(-0.18, 0.22)
Hedges' P-value		0.8470

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	140	146
Mean (SD)	86.85 (12.51)	86.70 (13.45)
Week 8 (MMRM)		
n	134	143
LS mean (SE)	86.83 (1.27)	86.21 (1.23)
95% CI of LS mean	(84.34, 89.32)	(83.80, 88.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.62 (-4.10, 2.86)
Absolute Change at Week 8 (MMRM)		
n	130	141
LS mean (SE)	-0.08 (1.28)	-0.57 (1.23)
95% CI of LS mean	(-2.60, 2.45)	(-3.00, 1.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.50 (-4.01, 3.01)
Week 16 (MMRM)		
n	129	139
LS mean (SE)	88.01 (1.19)	85.98 (1.15)
95% CI of LS mean	(85.67, 90.36)	(83.72, 88.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.03 (-5.30, 1.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 16 (MMRM)		
n	125	137
LS mean (SE)	0.99 (1.13)	-0.59 (1.08)
95% CI of LS mean	(-1.23, 3.22)	(-2.72, 1.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.58 (-4.67, 1.51)
Week 24 (MMRM)		
n	133	140
LS mean (SE)	86.25 (1.17)	84.83 (1.14)
95% CI of LS mean	(83.94, 88.55)	(82.59, 87.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.42 (-4.65, 1.82)
Absolute Change at Week 24 (MMRM)		
n	129	137
LS mean (SE)	-0.64 (1.23)	-1.62 (1.19)
95% CI of LS mean	(-3.06, 1.78)	(-3.96, 0.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.98 (-4.36, 2.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52		
n	139	143
Mean (SD)	85.95 (15.97)	88.90 (11.70)
Absolute Change at Week 52		
n	135	140
Mean (SD)	-1.03 (15.78)	2.45 (12.12)
Week 52 (MMRM)		
n	132	139
LS mean (SE)	85.74 (1.19)	88.86 (1.15)
95% CI of LS mean	(83.40, 88.07)	(86.58, 91.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.12 (-0.15, 6.39)
Absolute Change at Week 52 (MMRM)		
n	128	136
LS mean (SE)	-1.35 (1.23)	2.33 (1.19)
95% CI of LS mean	(-3.76, 1.07)	(-0.02, 4.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.67 (0.29, 7.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change through Week 52 (MMRM)		
n	130	139
LS mean (SE)	-0.33 (0.93)	0.04 (0.90)
95% CI of LS mean	(-2.16, 1.50)	(-1.73, 1.81)
P-value within Treatment	0.7223	0.9633
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.37 (-2.18, 2.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7750
Hedges' G (SE)		0.04 (0.12)
Hedges' 95% CI		(-0.20, 0.27)
Hedges' P-value		0.7738

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	142	134
Mean (SD)	84.42 (13.80)	84.63 (12.85)
Week 8 (MMRM)		
n	143	131
LS mean (SE)	83.71 (1.39)	82.83 (1.45)
95% CI of LS mean	(80.97, 86.46)	(79.96, 85.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.89 (-4.87, 3.09)
Absolute Change at Week 8 (MMRM)		
n	140	130
LS mean (SE)	-1.14 (1.50)	-1.75 (1.56)
95% CI of LS mean	(-4.10, 1.82)	(-4.82, 1.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.61 (-4.89, 3.67)
Week 16 (MMRM)		
n	143	129
LS mean (SE)	82.86 (1.51)	84.14 (1.59)
95% CI of LS mean	(79.88, 85.84)	(81.02, 87.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.28 (-3.04, 5.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 16 (MMRM)		
n	140	128
LS mean (SE)	-1.85 (1.55)	-0.43 (1.61)
95% CI of LS mean	(-4.91, 1.20)	(-3.61, 2.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.42 (-3.00, 5.84)
Week 24 (MMRM)		
n	141	125
LS mean (SE)	81.40 (1.44)	82.41 (1.53)
95% CI of LS mean	(78.56, 84.25)	(79.41, 85.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.01 (-3.14, 5.16)
Absolute Change at Week 24 (MMRM)		
n	138	125
LS mean (SE)	-3.35 (1.36)	-2.03 (1.42)
95% CI of LS mean	(-6.02, -0.68)	(-4.82, 0.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.32 (-2.56, 5.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52		
n	138	121
Mean (SD)	83.80 (17.82)	85.28 (14.49)
Absolute Change at Week 52		
n	135	120
Mean (SD)	-0.55 (18.75)	0.51 (14.76)
Week 52 (MMRM)		
n	137	119
LS mean (SE)	84.39 (1.34)	84.88 (1.43)
95% CI of LS mean	(81.75, 87.03)	(82.07, 87.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.49 (-3.38, 4.36)
Absolute Change at Week 52 (MMRM)		
n	134	118
LS mean (SE)	-0.29 (1.48)	0.38 (1.56)
95% CI of LS mean	(-3.20, 2.62)	(-2.70, 3.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.66 (-3.58, 4.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change through Week 52 (MMRM)		
n	140	129
LS mean (SE)	-1.83 (1.15)	-0.70 (1.20)
95% CI of LS mean	(-4.10, 0.44)	(-3.06, 1.67)
P-value within Treatment	0.1136	0.5634
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.13 (-2.17, 4.44)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4991
Hedges' G (SE)		0.08 (0.12)
Hedges' 95% CI		(-0.16, 0.32)
Hedges' P-value		0.4966

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	102	111
Mean (SD)	85.36 (12.71)	87.51 (12.23)
Week 8 (MMRM)		
n	98	112
LS mean (SE)	83.92 (1.50)	85.94 (1.40)
95% CI of LS mean	(80.96, 86.88)	(83.17, 88.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.03 (-2.03, 6.08)
Absolute Change at Week 8 (MMRM)		
n	97	109
LS mean (SE)	-1.46 (1.57)	-1.84 (1.48)
95% CI of LS mean	(-4.57, 1.64)	(-4.77, 1.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-4.65, 3.89)
Week 16 (MMRM)		
n	96	108
LS mean (SE)	85.84 (1.51)	86.36 (1.43)
95% CI of LS mean	(82.86, 88.82)	(83.55, 89.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.52 (-3.58, 4.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 16 (MMRM)		
n	95	105
LS mean (SE)	0.18 (1.36)	-1.28 (1.30)
95% CI of LS mean	(-2.51, 2.87)	(-3.84, 1.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.47 (-5.18, 2.25)
Week 24 (MMRM)		
n	98	108
LS mean (SE)	84.46 (1.50)	84.68 (1.43)
95% CI of LS mean	(81.50, 87.42)	(81.86, 87.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.22 (-3.87, 4.31)
Absolute Change at Week 24 (MMRM)		
n	97	106
LS mean (SE)	-0.86 (1.43)	-2.81 (1.37)
95% CI of LS mean	(-3.68, 1.96)	(-5.51, -0.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.95 (-5.86, 1.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52		
n	101	104
Mean (SD)	84.93 (15.91)	87.04 (13.88)
Absolute Change at Week 52		
n	100	101
Mean (SD)	-0.24 (15.48)	-0.51 (13.28)
Week 52 (MMRM)		
n	97	104
LS mean (SE)	84.59 (1.48)	86.65 (1.42)
95% CI of LS mean	(81.67, 87.51)	(83.84, 89.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.06 (-2.00, 6.12)
Absolute Change at Week 52 (MMRM)		
n	96	101
LS mean (SE)	-0.72 (1.49)	-0.64 (1.44)
95% CI of LS mean	(-3.65, 2.21)	(-3.49, 2.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-4.01, 4.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change through Week 52 (MMRM)		
n	98	107
LS mean (SE)	-0.47 (1.09)	-1.58 (1.05)
95% CI of LS mean	(-2.62, 1.69)	(-3.64, 0.48)
P-value within Treatment	0.6701	0.1321
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.11 (-4.10, 1.87)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4626
Hedges' G (SE)		-0.10 (0.14)
Hedges' 95% CI		(-0.38, 0.17)
Hedges' P-value		0.4620

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	180	169
Mean (SD)	85.77 (13.52)	84.53 (13.68)
Week 8 (MMRM)		
n	179	162
LS mean (SE)	85.80 (1.22)	83.81 (1.28)
95% CI of LS mean	(83.41, 88.19)	(81.30, 86.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.99 (-5.46, 1.48)
Absolute Change at Week 8 (MMRM)		
n	173	162
LS mean (SE)	-0.13 (1.27)	-0.70 (1.31)
95% CI of LS mean	(-2.62, 2.37)	(-3.28, 1.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.57 (-4.17, 3.02)
Week 16 (MMRM)		
n	176	160
LS mean (SE)	84.89 (1.27)	84.36 (1.33)
95% CI of LS mean	(82.40, 87.38)	(81.75, 86.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.53 (-4.14, 3.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	170	160
LS mean (SE)	-0.85 (1.30)	-0.12 (1.34)
95% CI of LS mean	(-3.40, 1.70)	(-2.75, 2.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.73 (-2.93, 4.40)
Week 24 (MMRM)		
n	176	157
LS mean (SE)	83.20 (1.19)	83.13 (1.26)
95% CI of LS mean	(80.86, 85.54)	(80.66, 85.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-3.47, 3.34)
Absolute Change at Week 24 (MMRM)		
n	170	156
LS mean (SE)	-2.68 (1.18)	-1.16 (1.23)
95% CI of LS mean	(-5.01, -0.36)	(-3.59, 1.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.52 (-1.84, 4.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52		
n	176	160
Mean (SD)	84.85 (17.52)	87.38 (12.70)
Absolute Change at Week 52		
n	170	159
Mean (SD)	-1.11 (18.32)	2.86 (13.37)
Week 52 (MMRM)		
n	172	154
LS mean (SE)	85.10 (1.13)	87.34 (1.19)
95% CI of LS mean	(82.88, 87.31)	(85.00, 89.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.24 (-0.99, 5.46)
Absolute Change at Week 52 (MMRM)		
n	166	153
LS mean (SE)	-0.83 (1.25)	2.79 (1.30)
95% CI of LS mean	(-3.29, 1.62)	(0.24, 5.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.63 (0.08, 7.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	172	161
LS mean (SE)	-1.46 (0.98)	0.50 (1.01)
95% CI of LS mean	(-3.38, 0.47)	(-1.49, 2.50)
P-value within Treatment	0.1375	0.6195
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.96 (-0.82, 4.74)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1657
Hedges' G (SE)		0.15 (0.11)
Hedges' 95% CI		(-0.06, 0.37)
Hedges' P-value		0.1656

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.2.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.4359
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	96.30 (4.54)	87.04 (11.56)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	93.75 (6.11)	87.04 (8.65)
95% CI of LS mean	(78.32, 109.18)	(65.58, 108.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.71 (-33.47, 20.05)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	N/C	N/C
95% CI of LS mean	N/C	N/C
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	N/C
Week 16 (MMRM)		
n	4	3
LS mean (SE)	90.09 (10.18)	83.50 (14.25)
95% CI of LS mean	(64.97, 115.21)	(48.78, 118.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.59 (-49.65, 36.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	N/C	N/C
95% CI of LS mean	N/C	N/C
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	N/C
Week 24 (MMRM)		
n	6	5
LS mean (SE)	95.05 (4.98)	83.55 (5.57)
95% CI of LS mean	(83.77, 106.33)	(70.97, 96.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-11.50 (-28.89, 5.89)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	N/C	N/C
95% CI of LS mean	N/C	N/C
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	94.92 (6.38)	95.37 (4.18)
Absolute Change at Week 52		
n	5	3
Mean (SD)	-0.44 (9.18)	5.56 (11.11)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	95.61 (2.47)	95.69 (2.47)
95% CI of LS mean	(89.73, 101.48)	(89.81, 101.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-9.10, 9.26)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	N/C	N/C
95% CI of LS mean	N/C	N/C
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	N/C	N/C
95% CI of LS mean	N/C	N/C
P-value within Treatment	N/C	N/C
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	N/C
Hedges' G (SE)		-
Hedges' 95% CI		-
Hedges' P-value		-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	93.33 (8.16)	91.85 (9.23)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	92.20 (4.71)	91.49 (3.83)
95% CI of LS mean	(81.47, 102.94)	(82.76, 100.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.71 (-14.66, 13.25)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	-0.53 (6.15)	-0.76 (5.01)
95% CI of LS mean	(-14.07, 13.01)	(-11.80, 10.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-17.77, 17.32)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	92.15 (4.37)	90.81 (3.45)
95% CI of LS mean	(82.41, 101.88)	(83.04, 98.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.34 (-14.00, 11.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	0.02 (3.85)	-1.28 (3.09)
95% CI of LS mean	(-8.80, 8.84)	(-8.37, 5.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.30 (-12.81, 10.21)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	92.39 (10.01)	83.44 (8.34)
95% CI of LS mean	(70.70, 114.08)	(65.44, 101.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.94 (-37.19, 19.31)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	-0.34 (9.20)	-8.24 (7.94)
95% CI of LS mean	(-20.36, 19.67)	(-25.43, 8.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.89 (-34.33, 18.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	98.61 (2.78)	94.44 (8.49)
Absolute Change at Week 52		
n	4	7
Mean (SD)	1.67 (3.33)	0.95 (6.10)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	99.59 (3.83)	93.26 (3.01)
95% CI of LS mean	(90.63, 108.54)	(86.15, 100.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.33 (-17.94, 5.29)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	5.04 (4.71)	-1.16 (3.77)
95% CI of LS mean	(-5.56, 15.64)	(-9.66, 7.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.20 (-19.91, 7.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	1.57 (4.92)	-3.56 (4.11)
95% CI of LS mean	(-9.35, 12.49)	(-12.63, 5.52)
P-value within Treatment	0.7556	0.4059
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.13 (-19.45, 9.18)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4453
Hedges' G (SE)		-0.39 (0.50)
Hedges' 95% CI		(-1.48, 0.69)
Hedges' P-value		0.4450

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.6319
Age at screening (<18 years vs. ≥18 years) [2]	0.2999
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.0528
Sex (Male vs. Female) [1]	0.0161
Region (North America vs. Rest of the World) [1]	0.8232

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.2019
Age at screening (<18 years vs. ≥18 years) [2]	0.8180
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.2752
Sex (Male vs. Female) [1]	0.5075
Region (North America vs. Rest of the World) [1]	0.0949

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

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Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.6339
Age at screening (<18 years vs. ≥18 years) [2]	0.1101
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.5833
Sex (Male vs. Female) [1]	0.4969
Region (North America vs. Rest of the World) [1]	0.1146

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

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Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.2508
Age at screening (<18 years vs. ≥18 years) [2]	0.6351
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.5208
Sex (Male vs. Female) [1]	0.7593
Region (North America vs. Rest of the World) [1]	0.2486

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.7356
Age at screening (<18 years vs. ≥18 years) [2]	0.6487
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.3043
Sex (Male vs. Female) [1]	0.3521
Region (North America vs. Rest of the World) [1]	0.1670

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

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Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.2161
Age at screening (<18 years vs. ≥18 years) [2]	0.2101
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.2073
Sex (Male vs. Female) [1]	0.9410
Region (North America vs. Rest of the World) [1]	0.2415

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

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Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.6302
Age at screening (<18 years vs. ≥18 years) [2]	0.6326
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.6606
Sex (Male vs. Female) [1]	0.6202
Region (North America vs. Rest of the World) [1]	0.6124

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

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Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.4732
Age at screening (<18 years vs. ≥18 years) [2]	0.3240
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.8155
Sex (Male vs. Female) [1]	0.7819
Region (North America vs. Rest of the World) [1]	0.7232

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

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Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.8734
Age at screening (<18 years vs. ≥18 years) [2]	0.0150
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.5255
Sex (Male vs. Female) [1]	0.6513
Region (North America vs. Rest of the World) [1]	0.8885

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

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Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.4107
Age at screening (<18 years vs. ≥18 years) [2]	0.3491
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.6407
Sex (Male vs. Female) [1]	0.7303
Region (North America vs. Rest of the World) [1]	0.2823

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

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Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1121
Age at screening (<18 years vs. ≥18 years) [2]	0.8145
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.7648
Sex (Male vs. Female) [1]	0.5029
Region (North America vs. Rest of the World) [1]	0.0303

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	164	152
Mean (SD)	75.27 (24.35)	78.65 (21.07)
Week 8 (MMRM)		
n	161	153
LS mean (SE)	76.75 (1.86)	78.49 (1.91)
95% CI of LS mean	(73.10, 80.41)	(74.74, 82.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.74 (-3.50, 6.98)
Absolute Change at Week 8 (MMRM)		
n	158	151
LS mean (SE)	1.86 (1.24)	0.12 (1.27)
95% CI of LS mean	(-0.59, 4.31)	(-2.39, 2.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.74 (-5.25, 1.76)
Week 16 (MMRM)		
n	158	148
LS mean (SE)	77.07 (1.66)	79.95 (1.71)
95% CI of LS mean	(73.79, 80.34)	(76.59, 83.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.88 (-1.82, 7.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 16 (MMRM)		
n	155	146
LS mean (SE)	1.75 (1.19)	1.33 (1.22)
95% CI of LS mean	(-0.59, 4.09)	(-1.08, 3.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.42 (-3.78, 2.93)
Week 24 (MMRM)		
n	156	147
LS mean (SE)	78.40 (1.72)	79.56 (1.77)
95% CI of LS mean	(75.02, 81.78)	(76.09, 83.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.16 (-3.69, 6.02)
Absolute Change at Week 24 (MMRM)		
n	153	145
LS mean (SE)	3.18 (1.22)	1.09 (1.25)
95% CI of LS mean	(0.77, 5.58)	(-1.38, 3.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.09 (-5.54, 1.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52		
n	159	145
Mean (SD)	77.99 (21.85)	79.62 (22.57)
Absolute Change at Week 52		
n	156	143
Mean (SD)	2.28 (17.97)	1.40 (17.34)
Week 52 (MMRM)		
n	155	144
LS mean (SE)	77.14 (1.76)	79.82 (1.82)
95% CI of LS mean	(73.67, 80.61)	(76.24, 83.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.68 (-2.31, 7.67)
Absolute Change at Week 52 (MMRM)		
n	152	142
LS mean (SE)	1.70 (1.43)	1.47 (1.47)
95% CI of LS mean	(-1.10, 4.51)	(-1.43, 4.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-4.27, 3.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	2.21 (1.08)	1.29 (1.11)
95% CI of LS mean	(0.08, 4.34)	(-0.89, 3.48)
P-value within Treatment	0.0419	0.2451
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.92 (-3.97, 2.14)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5550
Hedges' G (SE)		-0.07 (0.11)
Hedges' 95% CI		(-0.29, 0.16)
Hedges' P-value		0.5548

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	115	123
Mean (SD)	77.29 (22.44)	79.04 (21.63)
Week 8 (MMRM)		
n	116	120
LS mean (SE)	80.94 (1.88)	80.34 (1.84)
95% CI of LS mean	(77.23, 84.65)	(76.72, 83.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.60 (-5.80, 4.60)
Absolute Change at Week 8 (MMRM)		
n	112	119
LS mean (SE)	3.23 (1.25)	1.12 (1.21)
95% CI of LS mean	(0.78, 5.69)	(-1.26, 3.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.12 (-5.54, 1.31)
Week 16 (MMRM)		
n	115	119
LS mean (SE)	80.28 (1.91)	79.09 (1.87)
95% CI of LS mean	(76.52, 84.04)	(75.41, 82.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.19 (-6.47, 4.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 16 (MMRM)		
n	111	118
LS mean (SE)	2.64 (1.24)	-0.06 (1.20)
95% CI of LS mean	(0.19, 5.09)	(-2.43, 2.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.70 (-6.12, 0.72)
Week 24 (MMRM)		
n	118	118
LS mean (SE)	80.43 (2.02)	79.90 (1.99)
95% CI of LS mean	(76.44, 84.42)	(75.98, 83.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.53 (-6.14, 5.08)
Absolute Change at Week 24 (MMRM)		
n	114	117
LS mean (SE)	3.06 (1.44)	0.82 (1.41)
95% CI of LS mean	(0.23, 5.89)	(-1.95, 3.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.24 (-6.21, 1.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52		
n	115	116
Mean (SD)	80.10 (19.94)	79.89 (20.82)
Absolute Change at Week 52		
n	111	114
Mean (SD)	2.70 (15.87)	1.36 (15.65)
Week 52 (MMRM)		
n	114	115
LS mean (SE)	80.30 (1.88)	80.43 (1.85)
95% CI of LS mean	(76.59, 84.01)	(76.78, 84.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-5.09, 5.35)
Absolute Change at Week 52 (MMRM)		
n	110	113
LS mean (SE)	2.95 (1.49)	1.31 (1.46)
95% CI of LS mean	(0.01, 5.89)	(-1.57, 4.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.64 (-5.76, 2.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change through Week 52 (MMRM)		
n	114	120
LS mean (SE)	2.88 (1.17)	0.69 (1.13)
95% CI of LS mean	(0.59, 5.18)	(-1.55, 2.93)
P-value within Treatment	0.0141	0.5440
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.19 (-5.41, 1.02)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1800
Hedges' G (SE)		-0.18 (0.13)
Hedges' 95% CI		(-0.43, 0.08)
Hedges' P-value		0.1796

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	37	40
Mean (SD)	77.48 (27.78)	83.89 (23.19)
Week 8 (MMRM)		
n	34	36
LS mean (SE)	82.31 (3.89)	84.58 (3.71)
95% CI of LS mean	(74.55, 90.07)	(77.18, 91.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.27 (-8.52, 13.06)
Absolute Change at Week 8 (MMRM)		
n	33	36
LS mean (SE)	4.32 (2.47)	0.07 (2.35)
95% CI of LS mean	(-0.61, 9.25)	(-4.61, 4.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.24 (-11.09, 2.61)
Week 16 (MMRM)		
n	32	36
LS mean (SE)	80.60 (4.02)	83.53 (3.80)
95% CI of LS mean	(72.59, 88.62)	(75.94, 91.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.92 (-8.19, 14.04)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 16 (MMRM)		
n	31	36
LS mean (SE)	2.99 (2.70)	-0.91 (2.53)
95% CI of LS mean	(-2.40, 8.37)	(-5.96, 4.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.90 (-11.33, 3.54)
Week 24 (MMRM)		
n	34	36
LS mean (SE)	81.10 (4.33)	82.43 (4.12)
95% CI of LS mean	(72.45, 89.75)	(74.20, 90.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.33 (-10.67, 13.33)
Absolute Change at Week 24 (MMRM)		
n	33	35
LS mean (SE)	3.96 (3.23)	-1.96 (3.07)
95% CI of LS mean	(-2.48, 10.40)	(-8.10, 4.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.92 (-14.86, 3.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52		
n	33	35
Mean (SD)	80.47 (20.98)	83.17 (22.45)
Absolute Change at Week 52		
n	32	34
Mean (SD)	1.74 (24.30)	-1.63 (20.68)
Week 52 (MMRM)		
n	32	35
LS mean (SE)	78.99 (3.77)	83.51 (3.60)
95% CI of LS mean	(71.46, 86.53)	(76.32, 90.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.51 (-5.97, 15.00)
Absolute Change at Week 52 (MMRM)		
n	31	34
LS mean (SE)	1.60 (4.09)	-1.29 (3.89)
95% CI of LS mean	(-6.56, 9.77)	(-9.05, 6.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.90 (-14.19, 8.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change through Week 52 (MMRM)		
n	33	38
LS mean (SE)	2.85 (2.93)	-1.39 (2.77)
95% CI of LS mean	(-3.00, 8.70)	(-6.92, 4.14)
P-value within Treatment	0.3341	0.6176
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.24 (-12.34, 3.86)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2997
Hedges' G (SE)		-0.25 (0.24)
Hedges' 95% CI		(-0.72, 0.22)
Hedges' P-value		0.2990

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	75.56 (23.02)	77.73 (21.02)
Week 8 (MMRM)		
n	243	237
LS mean (SE)	77.98 (1.42)	78.47 (1.44)
95% CI of LS mean	(75.19, 80.76)	(75.64, 81.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.49 (-3.48, 4.46)
Absolute Change at Week 8 (MMRM)		
n	237	234
LS mean (SE)	2.16 (0.95)	0.66 (0.95)
95% CI of LS mean	(0.29, 4.02)	(-1.21, 2.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.50 (-4.14, 1.15)
Week 16 (MMRM)		
n	241	231
LS mean (SE)	78.01 (1.32)	78.89 (1.34)
95% CI of LS mean	(75.42, 80.60)	(76.25, 81.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.88 (-2.82, 4.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 16 (MMRM)		
n	235	228
LS mean (SE)	2.00 (0.90)	0.94 (0.91)
95% CI of LS mean	(0.22, 3.77)	(-0.86, 2.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.06 (-3.58, 1.47)
Week 24 (MMRM)		
n	240	229
LS mean (SE)	78.88 (1.37)	79.27 (1.39)
95% CI of LS mean	(76.19, 81.57)	(76.53, 82.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.39 (-3.46, 4.23)
Absolute Change at Week 24 (MMRM)		
n	234	227
LS mean (SE)	2.98 (0.96)	1.44 (0.97)
95% CI of LS mean	(1.10, 4.86)	(-0.47, 3.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.54 (-4.23, 1.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52		
n	244	230
Mean (SD)	78.37 (21.12)	79.03 (21.74)
Absolute Change at Week 52		
n	238	227
Mean (SD)	2.61 (15.92)	1.76 (15.75)
Week 52 (MMRM)		
n	237	224
LS mean (SE)	78.35 (1.37)	79.52 (1.39)
95% CI of LS mean	(75.66, 81.04)	(76.78, 82.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-2.67, 5.01)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	2.29 (1.04)	1.81 (1.06)
95% CI of LS mean	(0.24, 4.34)	(-0.27, 3.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.48 (-3.40, 2.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	2.42 (0.81)	1.40 (0.82)
95% CI of LS mean	(0.83, 4.01)	(-0.21, 3.01)
P-value within Treatment	0.0029	0.0885
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.03 (-3.29, 1.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3738
Hedges' G (SE)		-0.08 (0.09)
Hedges' 95% CI		(-0.26, 0.10)
Hedges' P-value		0.3734

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	78	71
Mean (SD)	75.64 (21.94)	83.26 (20.22)
Week 8 (MMRM)		
n	79	68
LS mean (SE)	80.76 (2.56)	79.30 (2.75)
95% CI of LS mean	(75.70, 85.82)	(73.88, 84.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.45 (-8.89, 5.98)
Absolute Change at Week 8 (MMRM)		
n	77	67
LS mean (SE)	4.24 (1.74)	-3.56 (1.86)
95% CI of LS mean	(0.81, 7.67)	(-7.23, 0.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.80 (-12.85, -2.76)
Week 16 (MMRM)		
n	77	67
LS mean (SE)	80.09 (2.22)	83.59 (2.38)
95% CI of LS mean	(75.71, 84.48)	(78.88, 88.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.49 (-2.95, 9.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 16 (MMRM)		
n	75	66
LS mean (SE)	3.68 (1.63)	0.86 (1.74)
95% CI of LS mean	(0.46, 6.89)	(-2.57, 4.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.82 (-7.54, 1.90)
Week 24 (MMRM)		
n	79	63
LS mean (SE)	79.07 (2.35)	82.33 (2.56)
95% CI of LS mean	(74.42, 83.72)	(77.28, 87.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.26 (-3.62, 10.14)
Absolute Change at Week 24 (MMRM)		
n	77	63
LS mean (SE)	2.80 (1.88)	-0.38 (2.05)
95% CI of LS mean	(-0.92, 6.52)	(-4.42, 3.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.18 (-8.68, 2.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52		
n	78	67
Mean (SD)	79.91 (20.89)	82.09 (22.22)
Absolute Change at Week 52		
n	76	66
Mean (SD)	4.24 (17.77)	-0.51 (17.91)
Week 52 (MMRM)		
n	77	64
LS mean (SE)	80.21 (2.40)	83.05 (2.60)
95% CI of LS mean	(75.46, 84.96)	(77.91, 88.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.83 (-4.18, 9.85)
Absolute Change at Week 52 (MMRM)		
n	75	63
LS mean (SE)	3.84 (2.08)	0.54 (2.25)
95% CI of LS mean	(-0.28, 7.95)	(-3.91, 5.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.29 (-9.37, 2.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change through Week 52 (MMRM)		
n	77	66
LS mean (SE)	3.44 (1.64)	0.34 (1.77)
95% CI of LS mean	(0.20, 6.68)	(-3.15, 3.83)
P-value within Treatment	0.0377	0.8467
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.10 (-7.88, 1.68)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2024
Hedges' G (SE)		-0.21 (0.17)
Hedges' 95% CI		(-0.55, 0.12)
Hedges' P-value		0.2020

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	197	207
Mean (SD)	75.75 (24.25)	77.03 (21.61)
Week 8 (MMRM)		
n	198	205
LS mean (SE)	77.63 (1.57)	79.28 (1.54)
95% CI of LS mean	(74.55, 80.71)	(76.26, 82.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.65 (-2.67, 5.97)
Absolute Change at Week 8 (MMRM)		
n	193	203
LS mean (SE)	1.64 (1.02)	1.98 (1.00)
95% CI of LS mean	(-0.36, 3.65)	(0.02, 3.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.34 (-2.47, 3.14)
Week 16 (MMRM)		
n	196	200
LS mean (SE)	77.73 (1.52)	78.23 (1.49)
95% CI of LS mean	(74.75, 80.72)	(75.29, 81.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-3.69, 4.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 16 (MMRM)		
n	191	198
LS mean (SE)	1.42 (1.01)	0.72 (0.99)
95% CI of LS mean	(-0.57, 3.41)	(-1.23, 2.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.70 (-3.49, 2.09)
Week 24 (MMRM)		
n	195	202
LS mean (SE)	79.32 (1.57)	78.85 (1.54)
95% CI of LS mean	(76.23, 82.40)	(75.82, 81.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-4.79, 3.86)
Absolute Change at Week 24 (MMRM)		
n	190	199
LS mean (SE)	3.19 (1.07)	1.51 (1.04)
95% CI of LS mean	(1.09, 5.29)	(-0.54, 3.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.68 (-4.62, 1.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52		
n	194	196
Mean (SD)	77.84 (21.08)	78.68 (21.74)
Absolute Change at Week 52		
n	189	193
Mean (SD)	1.53 (16.77)	1.90 (16.02)
Week 52 (MMRM)		
n	192	195
LS mean (SE)	77.78 (1.53)	79.12 (1.51)
95% CI of LS mean	(74.77, 80.79)	(76.16, 82.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.34 (-2.88, 5.57)
Absolute Change at Week 52 (MMRM)		
n	187	192
LS mean (SE)	1.50 (1.19)	1.80 (1.17)
95% CI of LS mean	(-0.84, 3.85)	(-0.51, 4.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.29 (-3.00, 3.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change through Week 52 (MMRM)		
n	193	202
LS mean (SE)	2.04 (0.90)	1.34 (0.88)
95% CI of LS mean	(0.26, 3.81)	(-0.39, 3.08)
P-value within Treatment	0.0245	0.1289
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.70 (-3.18, 1.79)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5826
Hedges' G (SE)		-0.06 (0.10)
Hedges' 95% CI		(-0.25, 0.14)
Hedges' P-value		0.5825

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	140	146
Mean (SD)	73.97 (24.89)	78.23 (22.90)
Week 8 (MMRM)		
n	134	143
LS mean (SE)	77.70 (2.01)	76.59 (1.95)
95% CI of LS mean	(73.74, 81.67)	(72.76, 80.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.11 (-6.66, 4.44)
Absolute Change at Week 8 (MMRM)		
n	130	141
LS mean (SE)	3.46 (1.13)	-1.73 (1.08)
95% CI of LS mean	(1.24, 5.68)	(-3.86, 0.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.18 (-8.28, -2.09)
Week 16 (MMRM)		
n	130	138
LS mean (SE)	77.09 (1.93)	77.99 (1.87)
95% CI of LS mean	(73.28, 80.89)	(74.30, 81.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.90 (-4.43, 6.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 16 (MMRM)		
n	126	136
LS mean (SE)	3.02 (1.16)	-0.55 (1.11)
95% CI of LS mean	(0.74, 5.29)	(-2.74, 1.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.57 (-6.74, -0.39)
Week 24 (MMRM)		
n	133	140
LS mean (SE)	78.04 (2.03)	78.40 (1.97)
95% CI of LS mean	(74.05, 82.04)	(74.53, 82.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-5.24, 5.96)
Absolute Change at Week 24 (MMRM)		
n	129	137
LS mean (SE)	4.22 (1.32)	0.11 (1.28)
95% CI of LS mean	(1.62, 6.81)	(-2.41, 2.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.11 (-7.74, -0.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52		
n	139	143
Mean (SD)	78.34 (21.04)	78.40 (23.73)
Absolute Change at Week 52		
n	135	140
Mean (SD)	4.44 (15.49)	0.79 (15.18)
Week 52 (MMRM)		
n	132	139
LS mean (SE)	78.02 (1.95)	79.19 (1.90)
95% CI of LS mean	(74.17, 81.87)	(75.46, 82.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-4.23, 6.57)
Absolute Change at Week 52 (MMRM)		
n	128	136
LS mean (SE)	4.02 (1.38)	0.91 (1.34)
95% CI of LS mean	(1.31, 6.74)	(-1.73, 3.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.12 (-6.91, 0.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change through Week 52 (MMRM)		
n	130	139
LS mean (SE)	3.75 (1.09)	0.15 (1.05)
95% CI of LS mean	(1.61, 5.90)	(-1.92, 2.23)
P-value within Treatment	0.0007	0.8835
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.60 (-6.60, -0.60)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0190
Hedges' G (SE)		-0.29 (0.12)
Hedges' 95% CI		(-0.53, -0.05)
Hedges' P-value		0.0190

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	142	134
Mean (SD)	77.62 (22.30)	79.02 (19.73)
Week 8 (MMRM)		
n	143	130
LS mean (SE)	79.54 (1.78)	81.97 (1.86)
95% CI of LS mean	(76.03, 83.05)	(78.30, 85.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.43 (-2.68, 7.53)
Absolute Change at Week 8 (MMRM)		
n	140	129
LS mean (SE)	1.48 (1.36)	2.96 (1.42)
95% CI of LS mean	(-1.20, 4.17)	(0.17, 5.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.48 (-2.41, 5.37)
Week 16 (MMRM)		
n	143	129
LS mean (SE)	79.85 (1.64)	81.03 (1.71)
95% CI of LS mean	(76.63, 83.07)	(77.67, 84.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.18 (-3.51, 5.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 16 (MMRM)		
n	140	128
LS mean (SE)	1.32 (1.28)	1.98 (1.33)
95% CI of LS mean	(-1.19, 3.84)	(-0.64, 4.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.65 (-3.00, 4.31)
Week 24 (MMRM)		
n	141	125
LS mean (SE)	80.62 (1.69)	80.91 (1.77)
95% CI of LS mean	(77.30, 83.94)	(77.43, 84.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.29 (-4.55, 5.14)
Absolute Change at Week 24 (MMRM)		
n	138	125
LS mean (SE)	2.16 (1.33)	1.85 (1.38)
95% CI of LS mean	(-0.45, 4.77)	(-0.87, 4.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-4.10, 3.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52		
n	138	122
Mean (SD)	78.90 (21.20)	80.97 (19.40)
Absolute Change at Week 52		
n	135	121
Mean (SD)	0.58 (18.38)	1.93 (17.90)
Week 52 (MMRM)		
n	137	120
LS mean (SE)	79.11 (1.72)	80.79 (1.81)
95% CI of LS mean	(75.72, 82.49)	(77.23, 84.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.69 (-3.26, 6.63)
Absolute Change at Week 52 (MMRM)		
n	134	119
LS mean (SE)	0.59 (1.56)	1.82 (1.63)
95% CI of LS mean	(-2.48, 3.65)	(-1.40, 5.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.24 (-3.22, 5.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change through Week 52 (MMRM)		
n	140	129
LS mean (SE)	1.36 (1.16)	1.88 (1.21)
95% CI of LS mean	(-0.94, 3.65)	(-0.50, 4.27)
P-value within Treatment	0.2452	0.1215
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.53 (-2.81, 3.86)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7559
Hedges' G (SE)		0.04 (0.12)
Hedges' 95% CI		(-0.20, 0.28)
Hedges' P-value		0.7543

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	102	111
Mean (SD)	75.82 (21.74)	80.98 (20.23)
Week 8 (MMRM)		
n	98	112
LS mean (SE)	78.43 (2.27)	80.66 (2.12)
95% CI of LS mean	(73.95, 82.90)	(76.47, 84.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.23 (-3.91, 8.37)
Absolute Change at Week 8 (MMRM)		
n	97	109
LS mean (SE)	2.47 (1.55)	-0.36 (1.46)
95% CI of LS mean	(-0.58, 5.53)	(-3.24, 2.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.83 (-7.04, 1.37)
Week 16 (MMRM)		
n	96	108
LS mean (SE)	77.94 (2.06)	82.34 (1.94)
95% CI of LS mean	(73.87, 82.00)	(78.53, 86.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.40 (-1.18, 9.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 16 (MMRM)		
n	95	105
LS mean (SE)	2.03 (1.40)	1.07 (1.33)
95% CI of LS mean	(-0.74, 4.80)	(-1.56, 3.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.96 (-4.78, 2.86)
Week 24 (MMRM)		
n	98	108
LS mean (SE)	78.70 (2.11)	80.99 (1.98)
95% CI of LS mean	(74.55, 82.86)	(77.08, 84.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.28 (-3.43, 8.00)
Absolute Change at Week 24 (MMRM)		
n	97	106
LS mean (SE)	2.92 (1.44)	-0.18 (1.37)
95% CI of LS mean	(0.09, 5.75)	(-2.88, 2.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.10 (-7.01, 0.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52		
n	101	104
Mean (SD)	77.45 (21.69)	80.56 (20.35)
Absolute Change at Week 52		
n	100	101
Mean (SD)	1.56 (18.08)	0.22 (15.31)
Week 52 (MMRM)		
n	97	104
LS mean (SE)	77.31 (2.11)	81.44 (2.00)
95% CI of LS mean	(73.15, 81.46)	(77.49, 85.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.13 (-1.61, 9.87)
Absolute Change at Week 52 (MMRM)		
n	96	101
LS mean (SE)	1.27 (1.70)	0.57 (1.64)
95% CI of LS mean	(-2.08, 4.62)	(-2.66, 3.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.70 (-5.36, 3.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change through Week 52 (MMRM)		
n	98	107
LS mean (SE)	2.07 (1.23)	0.49 (1.17)
95% CI of LS mean	(-0.35, 4.49)	(-1.82, 2.79)
P-value within Treatment	0.0928	0.6777
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.58 (-4.93, 1.76)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3519
Hedges' G (SE)		-0.13 (0.14)
Hedges' 95% CI		(-0.41, 0.14)
Hedges' P-value		0.3515

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	180	169
Mean (SD)	75.80 (24.72)	77.05 (22.06)
Week 8 (MMRM)		
n	179	161
LS mean (SE)	78.48 (1.65)	78.42 (1.73)
95% CI of LS mean	(75.24, 81.72)	(75.01, 81.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-4.77, 4.65)
Absolute Change at Week 8 (MMRM)		
n	173	161
LS mean (SE)	2.44 (1.08)	1.16 (1.12)
95% CI of LS mean	(0.31, 4.58)	(-1.04, 3.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.28 (-4.35, 1.79)
Week 16 (MMRM)		
n	177	159
LS mean (SE)	78.55 (1.57)	77.76 (1.65)
95% CI of LS mean	(75.47, 81.64)	(74.52, 81.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.79 (-5.27, 3.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	171	159
LS mean (SE)	2.17 (1.10)	0.45 (1.13)
95% CI of LS mean	(0.01, 4.33)	(-1.78, 2.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.71 (-4.82, 1.39)
Week 24 (MMRM)		
n	176	157
LS mean (SE)	79.43 (1.67)	78.97 (1.76)
95% CI of LS mean	(76.14, 82.73)	(75.51, 82.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-5.25, 4.32)
Absolute Change at Week 24 (MMRM)		
n	170	156
LS mean (SE)	3.22 (1.22)	1.75 (1.27)
95% CI of LS mean	(0.82, 5.62)	(-0.74, 4.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.47 (-4.93, 2.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52		
n	176	161
Mean (SD)	79.29 (20.76)	78.95 (22.79)
Absolute Change at Week 52		
n	170	160
Mean (SD)	3.07 (16.49)	2.01 (17.17)
Week 52 (MMRM)		
n	172	155
LS mean (SE)	79.03 (1.62)	79.28 (1.70)
95% CI of LS mean	(75.84, 82.22)	(75.93, 82.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.25 (-4.38, 4.88)
Absolute Change at Week 52 (MMRM)		
n	166	154
LS mean (SE)	2.78 (1.31)	1.96 (1.36)
95% CI of LS mean	(0.20, 5.36)	(-0.71, 4.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.82 (-4.53, 2.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	172	161
LS mean (SE)	2.72 (1.04)	1.39 (1.08)
95% CI of LS mean	(0.67, 4.77)	(-0.73, 3.51)
P-value within Treatment	0.0093	0.1984
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.33 (-4.29, 1.62)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3754
Hedges' G (SE)		-0.10 (0.11)
Hedges' 95% CI		(-0.31, 0.12)
Hedges' P-value		0.3749

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	164	152
Mean (SD)	79.95 (16.87)	82.97 (18.44)
Week 8 (MMRM)		
n	161	152
LS mean (SE)	79.97 (1.48)	81.52 (1.52)
95% CI of LS mean	(77.06, 82.88)	(78.52, 84.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.54 (-2.63, 5.72)
Absolute Change at Week 8 (MMRM)		
n	158	150
LS mean (SE)	0.72 (1.22)	-1.34 (1.25)
95% CI of LS mean	(-1.67, 3.11)	(-3.80, 1.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.07 (-5.49, 1.36)
Week 16 (MMRM)		
n	157	149
LS mean (SE)	78.66 (1.50)	80.97 (1.54)
95% CI of LS mean	(75.71, 81.62)	(77.94, 84.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.31 (-1.93, 6.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 16 (MMRM)		
n	154	147
LS mean (SE)	-0.72 (1.24)	-1.99 (1.27)
95% CI of LS mean	(-3.17, 1.72)	(-4.50, 0.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.27 (-4.77, 2.23)
Week 24 (MMRM)		
n	155	147
LS mean (SE)	80.04 (1.46)	80.72 (1.50)
95% CI of LS mean	(77.16, 82.92)	(77.76, 83.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.68 (-3.45, 4.80)
Absolute Change at Week 24 (MMRM)		
n	152	145
LS mean (SE)	0.99 (1.24)	-2.24 (1.27)
95% CI of LS mean	(-1.44, 3.43)	(-4.73, 0.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.23 (-6.71, 0.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52		
n	159	144
Mean (SD)	78.48 (19.99)	80.02 (17.85)
Absolute Change at Week 52		
n	156	142
Mean (SD)	-0.93 (16.45)	-2.90 (15.47)
Week 52 (MMRM)		
n	155	143
LS mean (SE)	78.08 (1.50)	80.19 (1.55)
95% CI of LS mean	(75.13, 81.04)	(77.14, 83.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.11 (-2.14, 6.36)
Absolute Change at Week 52 (MMRM)		
n	152	141
LS mean (SE)	-1.19 (1.30)	-2.71 (1.34)
95% CI of LS mean	(-3.75, 1.36)	(-5.35, -0.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.51 (-5.19, 2.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	-0.31 (1.07)	-2.31 (1.10)
95% CI of LS mean	(-2.41, 1.79)	(-4.47, -0.16)
P-value within Treatment	0.7726	0.0356
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.00 (-5.02, 1.01)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1917
Hedges' G (SE)		-0.15 (0.11)
Hedges' 95% CI		(-0.38, 0.08)
Hedges' P-value		0.1919

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	115	123
Mean (SD)	83.00 (17.31)	80.94 (18.58)
Week 8 (MMRM)		
n	116	121
LS mean (SE)	82.76 (1.70)	81.09 (1.66)
95% CI of LS mean	(79.42, 86.11)	(77.82, 84.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.68 (-6.37, 3.02)
Absolute Change at Week 8 (MMRM)		
n	112	120
LS mean (SE)	-0.69 (1.29)	0.10 (1.25)
95% CI of LS mean	(-3.24, 1.86)	(-2.36, 2.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.79 (-2.77, 4.34)
Week 16 (MMRM)		
n	115	119
LS mean (SE)	83.75 (1.66)	81.75 (1.63)
95% CI of LS mean	(80.47, 87.02)	(78.55, 84.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.99 (-6.59, 2.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 16 (MMRM)		
n	111	118
LS mean (SE)	0.54 (1.37)	0.67 (1.33)
95% CI of LS mean	(-2.16, 3.23)	(-1.94, 3.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-3.63, 3.90)
Week 24 (MMRM)		
n	118	118
LS mean (SE)	82.18 (1.90)	79.44 (1.87)
95% CI of LS mean	(78.44, 85.92)	(75.77, 83.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.74 (-8.00, 2.52)
Absolute Change at Week 24 (MMRM)		
n	114	117
LS mean (SE)	-1.23 (1.37)	-1.60 (1.34)
95% CI of LS mean	(-3.93, 1.47)	(-4.24, 1.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.37 (-4.16, 3.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52		
n	115	116
Mean (SD)	80.97 (20.85)	79.69 (20.63)
Absolute Change at Week 52		
n	111	114
Mean (SD)	-2.70 (14.54)	-1.56 (17.10)
Week 52 (MMRM)		
n	114	115
LS mean (SE)	80.42 (1.95)	79.82 (1.92)
95% CI of LS mean	(76.59, 84.26)	(76.04, 83.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.60 (-6.01, 4.80)
Absolute Change at Week 52 (MMRM)		
n	110	113
LS mean (SE)	-2.91 (1.53)	-1.34 (1.50)
95% CI of LS mean	(-5.92, 0.10)	(-4.30, 1.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.57 (-2.66, 5.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change through Week 52 (MMRM)		
n	114	120
LS mean (SE)	-1.20 (1.18)	-0.76 (1.15)
95% CI of LS mean	(-3.54, 1.13)	(-3.03, 1.52)
P-value within Treatment	0.3105	0.5122
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-2.82, 3.71)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7880
Hedges' G (SE)		0.04 (0.13)
Hedges' 95% CI		(-0.22, 0.29)
Hedges' P-value		0.7874

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	37	40
Mean (SD)	87.39 (15.97)	83.06 (21.79)
Week 8 (MMRM)		
n	34	37
LS mean (SE)	89.51 (3.10)	85.69 (2.95)
95% CI of LS mean	(83.34, 95.69)	(79.81, 91.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.82 (-12.41, 4.76)
Absolute Change at Week 8 (MMRM)		
n	33	37
LS mean (SE)	1.79 (2.83)	2.41 (2.68)
95% CI of LS mean	(-3.86, 7.43)	(-2.93, 7.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.62 (-7.21, 8.45)
Week 16 (MMRM)		
n	32	36
LS mean (SE)	92.42 (2.94)	89.39 (2.79)
95% CI of LS mean	(86.55, 98.30)	(83.82, 94.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.03 (-11.20, 5.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 16 (MMRM)		
n	31	36
LS mean (SE)	5.00 (3.15)	6.10 (2.95)
95% CI of LS mean	(-1.27, 11.28)	(0.21, 11.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.10 (-7.57, 9.76)
Week 24 (MMRM)		
n	34	36
LS mean (SE)	89.22 (3.28)	84.72 (3.14)
95% CI of LS mean	(82.68, 95.76)	(78.46, 90.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.50 (-13.61, 4.60)
Absolute Change at Week 24 (MMRM)		
n	33	35
LS mean (SE)	1.98 (3.01)	1.16 (2.89)
95% CI of LS mean	(-4.03, 7.99)	(-4.60, 6.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.82 (-9.19, 7.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52		
n	33	34
Mean (SD)	87.54 (17.29)	85.62 (18.66)
Absolute Change at Week 52		
n	32	33
Mean (SD)	0.69 (13.22)	-0.67 (24.21)
Week 52 (MMRM)		
n	32	34
LS mean (SE)	86.47 (3.37)	84.25 (3.24)
95% CI of LS mean	(79.72, 93.22)	(77.77, 90.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.22 (-11.63, 7.18)
Absolute Change at Week 52 (MMRM)		
n	31	33
LS mean (SE)	-1.01 (3.55)	0.49 (3.40)
95% CI of LS mean	(-8.11, 6.10)	(-6.31, 7.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.49 (-8.38, 11.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change through Week 52 (MMRM)		
n	33	38
LS mean (SE)	1.99 (2.79)	2.58 (2.64)
95% CI of LS mean	(-3.57, 7.55)	(-2.69, 7.85)
P-value within Treatment	0.4772	0.3319
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.59 (-7.13, 8.31)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8791
Hedges' G (SE)		0.04 (0.24)
Hedges' 95% CI		(-0.43, 0.51)
Hedges' P-value		0.8783

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	80.14 (17.14)	81.90 (17.81)
Week 8 (MMRM)		
n	243	236
LS mean (SE)	79.90 (1.19)	80.63 (1.21)
95% CI of LS mean	(77.55, 82.25)	(78.25, 83.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.74 (-2.61, 4.08)
Absolute Change at Week 8 (MMRM)		
n	237	233
LS mean (SE)	-0.21 (0.93)	-1.11 (0.94)
95% CI of LS mean	(-2.05, 1.62)	(-2.96, 0.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.90 (-3.51, 1.71)
Week 16 (MMRM)		
n	240	232
LS mean (SE)	79.06 (1.21)	79.97 (1.22)
95% CI of LS mean	(76.69, 81.43)	(77.57, 82.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.91 (-2.47, 4.30)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 16 (MMRM)		
n	234	229
LS mean (SE)	-1.07 (0.95)	-1.83 (0.96)
95% CI of LS mean	(-2.94, 0.80)	(-3.72, 0.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.76 (-3.42, 1.91)
Week 24 (MMRM)		
n	239	229
LS mean (SE)	79.67 (1.25)	79.37 (1.27)
95% CI of LS mean	(77.21, 82.12)	(76.88, 81.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.29 (-3.80, 3.21)
Absolute Change at Week 24 (MMRM)		
n	233	227
LS mean (SE)	-0.34 (0.96)	-2.44 (0.97)
95% CI of LS mean	(-2.22, 1.54)	(-4.34, -0.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.10 (-4.78, 0.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52		
n	244	230
Mean (SD)	78.51 (20.47)	78.94 (19.03)
Absolute Change at Week 52		
n	238	227
Mean (SD)	-1.77 (16.04)	-2.69 (14.66)
Week 52 (MMRM)		
n	237	224
LS mean (SE)	77.93 (1.28)	79.32 (1.31)
95% CI of LS mean	(75.42, 80.45)	(76.75, 81.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.39 (-2.21, 4.98)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	-2.20 (1.01)	-2.42 (1.03)
95% CI of LS mean	(-4.18, -0.21)	(-4.44, -0.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-3.06, 2.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	-1.20 (0.81)	-2.23 (0.82)
95% CI of LS mean	(-2.80, 0.40)	(-3.85, -0.61)
P-value within Treatment	0.1403	0.0072
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.02 (-3.30, 1.26)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3776
Hedges' G (SE)		-0.08 (0.09)
Hedges' 95% CI		(-0.26, 0.10)
Hedges' P-value		0.3771

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	78	71
Mean (SD)	80.91 (17.81)	82.79 (18.67)
Week 8 (MMRM)		
n	79	69
LS mean (SE)	81.81 (2.15)	80.57 (2.30)
95% CI of LS mean	(77.56, 86.06)	(76.02, 85.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.24 (-7.48, 5.00)
Absolute Change at Week 8 (MMRM)		
n	77	68
LS mean (SE)	0.61 (1.69)	-1.50 (1.80)
95% CI of LS mean	(-2.74, 3.95)	(-5.07, 2.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.11 (-7.02, 2.81)
Week 16 (MMRM)		
n	76	67
LS mean (SE)	81.02 (2.31)	79.42 (2.47)
95% CI of LS mean	(76.45, 85.58)	(74.53, 84.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.60 (-8.30, 5.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 16 (MMRM)		
n	74	66
LS mean (SE)	-0.32 (1.97)	-2.87 (2.10)
95% CI of LS mean	(-4.23, 3.58)	(-7.03, 1.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.55 (-8.27, 3.17)
Week 24 (MMRM)		
n	79	63
LS mean (SE)	82.51 (2.27)	80.50 (2.46)
95% CI of LS mean	(78.03, 87.00)	(75.64, 85.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.01 (-8.64, 4.62)
Absolute Change at Week 24 (MMRM)		
n	77	63
LS mean (SE)	1.18 (1.93)	-1.74 (2.08)
95% CI of LS mean	(-2.63, 4.99)	(-5.86, 2.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.92 (-8.55, 2.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52		
n	78	66
Mean (SD)	81.48 (20.55)	80.13 (18.54)
Absolute Change at Week 52		
n	76	65
Mean (SD)	-0.15 (15.77)	-3.59 (15.60)
Week 52 (MMRM)		
n	77	63
LS mean (SE)	81.37 (2.20)	79.93 (2.39)
95% CI of LS mean	(77.01, 85.73)	(75.21, 84.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.44 (-7.88, 5.00)
Absolute Change at Week 52 (MMRM)		
n	75	62
LS mean (SE)	-0.05 (1.87)	-2.52 (2.03)
95% CI of LS mean	(-3.74, 3.64)	(-6.53, 1.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.47 (-7.94, 2.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change through Week 52 (MMRM)		
n	77	66
LS mean (SE)	0.27 (1.68)	-2.38 (1.80)
95% CI of LS mean	(-3.04, 3.58)	(-5.93, 1.18)
P-value within Treatment	0.8720	0.1884
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.65 (-7.53, 2.23)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2853
Hedges' G (SE)		-0.18 (0.17)
Hedges' 95% CI		(-0.51, 0.15)
Hedges' P-value		0.2845

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	197	207
Mean (SD)	80.82 (16.97)	81.75 (18.38)
Week 8 (MMRM)		
n	198	204
LS mean (SE)	80.93 (1.31)	81.55 (1.29)
95% CI of LS mean	(78.35, 83.52)	(79.01, 84.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.62 (-3.01, 4.24)
Absolute Change at Week 8 (MMRM)		
n	193	202
LS mean (SE)	-0.12 (1.04)	-0.36 (1.02)
95% CI of LS mean	(-2.17, 1.93)	(-2.37, 1.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-3.12, 2.63)
Week 16 (MMRM)		
n	196	201
LS mean (SE)	80.72 (1.27)	81.91 (1.25)
95% CI of LS mean	(78.22, 83.21)	(79.46, 84.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.20 (-2.30, 4.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 16 (MMRM)		
n	191	199
LS mean (SE)	-0.24 (1.04)	-0.01 (1.02)
95% CI of LS mean	(-2.29, 1.80)	(-2.01, 1.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.23 (-2.63, 3.09)
Week 24 (MMRM)		
n	194	202
LS mean (SE)	80.31 (1.36)	80.07 (1.33)
95% CI of LS mean	(77.64, 82.99)	(77.44, 82.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-3.99, 3.50)
Absolute Change at Week 24 (MMRM)		
n	189	199
LS mean (SE)	-0.47 (1.04)	-1.88 (1.01)
95% CI of LS mean	(-2.51, 1.57)	(-3.87, 0.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.41 (-4.26, 1.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52		
n	194	196
Mean (SD)	78.41 (20.27)	79.65 (19.32)
Absolute Change at Week 52		
n	189	193
Mean (SD)	-2.18 (15.83)	-2.01 (16.41)
Week 52 (MMRM)		
n	192	195
LS mean (SE)	78.19 (1.42)	80.11 (1.40)
95% CI of LS mean	(75.40, 80.98)	(77.35, 82.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.91 (-2.01, 5.83)
Absolute Change at Week 52 (MMRM)		
n	187	192
LS mean (SE)	-2.70 (1.17)	-1.79 (1.15)
95% CI of LS mean	(-5.00, -0.40)	(-4.06, 0.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.91 (-2.32, 4.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change through Week 52 (MMRM)		
n	193	202
LS mean (SE)	-1.14 (0.90)	-1.23 (0.88)
95% CI of LS mean	(-2.90, 0.62)	(-2.95, 0.49)
P-value within Treatment	0.2049	0.1615
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-2.56, 2.38)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9417
Hedges' G (SE)		-0.01 (0.10)
Hedges' 95% CI		(-0.20, 0.19)
Hedges' P-value		0.9417

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	140	146
Mean (SD)	81.59 (16.47)	82.88 (17.99)
Week 8 (MMRM)		
n	134	142
LS mean (SE)	82.35 (1.49)	83.06 (1.45)
95% CI of LS mean	(79.42, 85.29)	(80.21, 85.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.70 (-3.41, 4.82)
Absolute Change at Week 8 (MMRM)		
n	130	140
LS mean (SE)	1.09 (1.27)	0.00 (1.22)
95% CI of LS mean	(-1.40, 3.59)	(-2.41, 2.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.10 (-4.58, 2.38)
Week 16 (MMRM)		
n	129	139
LS mean (SE)	80.66 (1.46)	82.66 (1.41)
95% CI of LS mean	(77.78, 83.53)	(79.87, 85.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.00 (-2.03, 6.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 16 (MMRM)		
n	125	137
LS mean (SE)	-0.45 (1.30)	-0.41 (1.25)
95% CI of LS mean	(-3.01, 2.11)	(-2.87, 2.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.04 (-3.53, 3.61)
Week 24 (MMRM)		
n	132	140
LS mean (SE)	80.58 (1.49)	82.70 (1.45)
95% CI of LS mean	(77.64, 83.52)	(79.85, 85.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.12 (-2.00, 6.25)
Absolute Change at Week 24 (MMRM)		
n	128	137
LS mean (SE)	-0.52 (1.21)	-0.44 (1.17)
95% CI of LS mean	(-2.91, 1.87)	(-2.75, 1.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-3.26, 3.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52		
n	139	143
Mean (SD)	80.02 (19.11)	81.74 (17.16)
Absolute Change at Week 52		
n	135	140
Mean (SD)	-1.48 (15.23)	-0.95 (15.63)
Week 52 (MMRM)		
n	132	139
LS mean (SE)	79.02 (1.57)	82.66 (1.53)
95% CI of LS mean	(75.92, 82.12)	(79.65, 85.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.64 (-0.70, 7.98)
Absolute Change at Week 52 (MMRM)		
n	128	136
LS mean (SE)	-2.26 (1.37)	-0.36 (1.33)
95% CI of LS mean	(-4.96, 0.43)	(-2.97, 2.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.90 (-1.86, 5.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change through Week 52 (MMRM)		
n	130	139
LS mean (SE)	-1.08 (1.07)	-0.40 (1.03)
95% CI of LS mean	(-3.18, 1.02)	(-2.43, 1.63)
P-value within Treatment	0.3136	0.6951
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.67 (-2.27, 3.61)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6525
Hedges' G (SE)		0.06 (0.12)
Hedges' 95% CI		(-0.18, 0.29)
Hedges' P-value		0.6507

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	142	134
Mean (SD)	80.59 (17.82)	81.18 (18.84)
Week 8 (MMRM)		
n	143	131
LS mean (SE)	79.88 (1.66)	79.62 (1.73)
95% CI of LS mean	(76.61, 83.16)	(76.21, 83.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-5.02, 4.50)
Absolute Change at Week 8 (MMRM)		
n	140	130
LS mean (SE)	-1.00 (1.25)	-1.13 (1.29)
95% CI of LS mean	(-3.46, 1.45)	(-3.67, 1.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-3.68, 3.43)
Week 16 (MMRM)		
n	143	129
LS mean (SE)	80.74 (1.70)	80.01 (1.78)
95% CI of LS mean	(77.39, 84.09)	(76.51, 83.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.73 (-5.61, 4.15)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 16 (MMRM)		
n	140	128
LS mean (SE)	-0.21 (1.31)	-0.91 (1.36)
95% CI of LS mean	(-2.79, 2.37)	(-3.59, 1.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.70 (-4.44, 3.04)
Week 24 (MMRM)		
n	141	125
LS mean (SE)	81.07 (1.80)	77.61 (1.89)
95% CI of LS mean	(77.53, 84.61)	(73.90, 81.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.46 (-8.62, 1.70)
Absolute Change at Week 24 (MMRM)		
n	138	125
LS mean (SE)	0.30 (1.37)	-3.27 (1.43)
95% CI of LS mean	(-2.39, 3.00)	(-6.09, -0.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.58 (-7.50, 0.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52		
n	138	121
Mean (SD)	79.15 (21.50)	77.50 (20.96)
Absolute Change at Week 52		
n	135	120
Mean (SD)	-1.48 (16.28)	-4.17 (16.62)
Week 52 (MMRM)		
n	137	119
LS mean (SE)	78.93 (1.80)	77.25 (1.90)
95% CI of LS mean	(75.38, 82.49)	(73.51, 81.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.68 (-6.87, 3.51)
Absolute Change at Week 52 (MMRM)		
n	134	118
LS mean (SE)	-1.83 (1.42)	-3.74 (1.50)
95% CI of LS mean	(-4.63, 0.97)	(-6.69, -0.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.91 (-5.99, 2.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change through Week 52 (MMRM)		
n	140	129
LS mean (SE)	-0.58 (1.16)	-2.64 (1.21)
95% CI of LS mean	(-2.87, 1.72)	(-5.03, -0.25)
P-value within Treatment	0.6203	0.0304
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.06 (-5.40, 1.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2240
Hedges' G (SE)		-0.15 (0.12)
Hedges' 95% CI		(-0.39, 0.09)
Hedges' P-value		0.2217

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	102	111
Mean (SD)	79.52 (17.74)	83.58 (18.46)
Week 8 (MMRM)		
n	98	112
LS mean (SE)	79.37 (1.85)	84.65 (1.73)
95% CI of LS mean	(75.73, 83.02)	(81.24, 88.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.28 (0.28, 10.28)
Absolute Change at Week 8 (MMRM)		
n	97	109
LS mean (SE)	-0.34 (1.34)	1.05 (1.27)
95% CI of LS mean	(-2.99, 2.30)	(-1.45, 3.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.39 (-2.25, 5.03)
Week 16 (MMRM)		
n	96	108
LS mean (SE)	79.15 (1.78)	84.79 (1.68)
95% CI of LS mean	(75.63, 82.66)	(81.49, 88.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.65 (0.81, 10.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 16 (MMRM)		
n	95	105
LS mean (SE)	-0.39 (1.50)	0.91 (1.43)
95% CI of LS mean	(-3.35, 2.58)	(-1.91, 3.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.29 (-2.80, 5.39)
Week 24 (MMRM)		
n	98	108
LS mean (SE)	80.24 (1.93)	83.85 (1.82)
95% CI of LS mean	(76.43, 84.05)	(80.26, 87.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.61 (-1.63, 8.86)
Absolute Change at Week 24 (MMRM)		
n	97	106
LS mean (SE)	0.77 (1.47)	-0.04 (1.40)
95% CI of LS mean	(-2.12, 3.67)	(-2.80, 2.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.81 (-4.82, 3.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52		
n	101	104
Mean (SD)	77.89 (20.21)	83.65 (17.51)
Absolute Change at Week 52		
n	100	101
Mean (SD)	-1.78 (16.01)	0.22 (15.31)
Week 52 (MMRM)		
n	97	104
LS mean (SE)	77.24 (1.91)	84.24 (1.82)
95% CI of LS mean	(73.47, 81.01)	(80.66, 87.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.00 (1.80, 12.20)
Absolute Change at Week 52 (MMRM)		
n	96	101
LS mean (SE)	-2.51 (1.57)	0.53 (1.52)
95% CI of LS mean	(-5.61, 0.58)	(-2.46, 3.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.04 (-1.27, 7.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change through Week 52 (MMRM)		
n	98	107
LS mean (SE)	-0.71 (1.26)	0.47 (1.21)
95% CI of LS mean	(-3.20, 1.79)	(-1.91, 2.85)
P-value within Treatment	0.5761	0.6999
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-2.28, 4.63)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5033
Hedges' G (SE)		0.09 (0.14)
Hedges' 95% CI		(-0.18, 0.37)
Hedges' P-value		0.5028

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	180	169
Mean (SD)	81.98 (16.78)	81.07 (18.33)
Week 8 (MMRM)		
n	179	161
LS mean (SE)	82.15 (1.39)	78.99 (1.46)
95% CI of LS mean	(79.41, 84.89)	(76.11, 81.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.16 (-7.14, 0.82)
Absolute Change at Week 8 (MMRM)		
n	173	161
LS mean (SE)	0.38 (1.15)	-1.82 (1.20)
95% CI of LS mean	(-1.89, 2.65)	(-4.17, 0.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.20 (-5.47, 1.08)
Week 16 (MMRM)		
n	176	160
LS mean (SE)	81.76 (1.42)	78.90 (1.49)
95% CI of LS mean	(78.97, 84.55)	(75.97, 81.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.86 (-6.92, 1.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	170	160
LS mean (SE)	-0.12 (1.14)	-1.90 (1.18)
95% CI of LS mean	(-2.37, 2.13)	(-4.23, 0.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.79 (-5.03, 1.45)
Week 24 (MMRM)		
n	175	157
LS mean (SE)	81.33 (1.46)	77.61 (1.53)
95% CI of LS mean	(78.47, 84.19)	(74.60, 80.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.72 (-7.87, 0.44)
Absolute Change at Week 24 (MMRM)		
n	169	156
LS mean (SE)	-0.42 (1.15)	-3.22 (1.20)
95% CI of LS mean	(-2.69, 1.84)	(-5.57, -0.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.79 (-6.06, 0.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52		
n	176	160
Mean (SD)	80.56 (20.35)	77.29 (19.68)
Absolute Change at Week 52		
n	170	159
Mean (SD)	-1.31 (15.61)	-4.12 (16.47)
Week 52 (MMRM)		
n	172	154
LS mean (SE)	80.12 (1.51)	77.13 (1.59)
95% CI of LS mean	(77.15, 83.09)	(74.00, 80.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.99 (-7.31, 1.32)
Absolute Change at Week 52 (MMRM)		
n	166	153
LS mean (SE)	-1.61 (1.25)	-3.79 (1.30)
95% CI of LS mean	(-4.07, 0.85)	(-6.35, -1.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.18 (-5.73, 1.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	172	161
LS mean (SE)	-0.72 (0.99)	-2.97 (1.02)
95% CI of LS mean	(-2.66, 1.23)	(-4.98, -0.95)
P-value within Treatment	0.4691	0.0040
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.25 (-5.06, 0.56)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1156
Hedges' G (SE)		-0.17 (0.11)
Hedges' 95% CI		(-0.39, 0.04)
Hedges' P-value		0.1156

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	164	152
Mean (SD)	92.78 (13.34)	94.15 (12.13)
Week 8 (MMRM)		
n	161	153
LS mean (SE)	91.88 (1.09)	93.87 (1.12)
95% CI of LS mean	(89.74, 94.03)	(91.67, 96.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.99 (-1.09, 5.06)
Absolute Change at Week 8 (MMRM)		
n	158	151
LS mean (SE)	-0.42 (0.87)	-0.34 (0.89)
95% CI of LS mean	(-2.12, 1.29)	(-2.08, 1.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-2.36, 2.52)
Week 16 (MMRM)		
n	158	149
LS mean (SE)	91.93 (1.10)	93.27 (1.13)
95% CI of LS mean	(89.76, 94.11)	(91.03, 95.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.33 (-1.79, 4.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 16 (MMRM)		
n	155	147
LS mean (SE)	-0.29 (0.87)	-0.93 (0.89)
95% CI of LS mean	(-2.01, 1.42)	(-2.69, 0.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-3.09, 1.81)
Week 24 (MMRM)		
n	156	147
LS mean (SE)	92.24 (1.13)	93.01 (1.16)
95% CI of LS mean	(90.01, 94.46)	(90.72, 95.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.78 (-2.42, 3.98)
Absolute Change at Week 24 (MMRM)		
n	153	145
LS mean (SE)	0.07 (0.83)	-1.17 (0.85)
95% CI of LS mean	(-1.55, 1.70)	(-2.84, 0.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.24 (-3.58, 1.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52		
n	159	145
Mean (SD)	93.01 (14.55)	93.26 (13.50)
Absolute Change at Week 52		
n	156	143
Mean (SD)	0.75 (13.16)	-0.93 (10.75)
Week 52 (MMRM)		
n	155	144
LS mean (SE)	92.83 (1.12)	93.31 (1.16)
95% CI of LS mean	(90.63, 95.03)	(91.04, 95.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.48 (-2.68, 3.65)
Absolute Change at Week 52 (MMRM)		
n	152	142
LS mean (SE)	0.47 (0.99)	-0.88 (1.02)
95% CI of LS mean	(-1.47, 2.41)	(-2.88, 1.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.35 (-4.13, 1.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	0.08 (0.70)	-0.99 (0.72)
95% CI of LS mean	(-1.29, 1.45)	(-2.40, 0.41)
P-value within Treatment	0.9055	0.1661
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.08 (-3.04, 0.89)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2827
Hedges' G (SE)		-0.12 (0.11)
Hedges' 95% CI		(-0.35, 0.10)
Hedges' P-value		0.2826

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	115	123
Mean (SD)	92.66 (16.11)	94.17 (11.96)
Week 8 (MMRM)		
n	116	121
LS mean (SE)	93.44 (1.27)	94.30 (1.24)
95% CI of LS mean	(90.93, 95.94)	(91.85, 96.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.86 (-2.65, 4.37)
Absolute Change at Week 8 (MMRM)		
n	112	120
LS mean (SE)	0.93 (1.04)	0.13 (1.00)
95% CI of LS mean	(-1.12, 2.98)	(-1.85, 2.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.80 (-3.66, 2.05)
Week 16 (MMRM)		
n	115	119
LS mean (SE)	93.58 (1.42)	93.05 (1.39)
95% CI of LS mean	(90.79, 96.37)	(90.31, 95.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.53 (-4.45, 3.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 16 (MMRM)		
n	111	118
LS mean (SE)	0.99 (1.24)	-1.15 (1.20)
95% CI of LS mean	(-1.45, 3.44)	(-3.52, 1.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.14 (-5.55, 1.27)
Week 24 (MMRM)		
n	118	118
LS mean (SE)	92.79 (1.55)	92.01 (1.54)
95% CI of LS mean	(89.73, 95.85)	(88.99, 95.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.78 (-5.09, 3.54)
Absolute Change at Week 24 (MMRM)		
n	114	117
LS mean (SE)	-0.07 (1.36)	-2.22 (1.34)
95% CI of LS mean	(-2.74, 2.61)	(-4.85, 0.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.15 (-5.91, 1.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52		
n	115	116
Mean (SD)	92.95 (15.60)	93.39 (13.74)
Absolute Change at Week 52		
n	111	114
Mean (SD)	0.30 (13.52)	-1.22 (12.49)
Week 52 (MMRM)		
n	114	115
LS mean (SE)	92.91 (1.34)	93.59 (1.33)
95% CI of LS mean	(90.26, 95.56)	(90.98, 96.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.68 (-3.05, 4.41)
Absolute Change at Week 52 (MMRM)		
n	110	113
LS mean (SE)	0.18 (1.22)	-0.62 (1.20)
95% CI of LS mean	(-2.22, 2.59)	(-2.98, 1.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.80 (-4.18, 2.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change through Week 52 (MMRM)		
n	114	120
LS mean (SE)	0.37 (1.01)	-1.33 (0.99)
95% CI of LS mean	(-1.62, 2.36)	(-3.27, 0.61)
P-value within Treatment	0.7152	0.1785
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.70 (-4.49, 1.09)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2311
Hedges' G (SE)		-0.16 (0.13)
Hedges' 95% CI		(-0.41, 0.10)
Hedges' P-value		0.2306

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	37	40
Mean (SD)	95.50 (8.87)	93.89 (13.06)
Week 8 (MMRM)		
n	34	37
LS mean (SE)	95.39 (1.80)	95.11 (1.73)
95% CI of LS mean	(91.79, 98.99)	(91.66, 98.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.28 (-5.28, 4.71)
Absolute Change at Week 8 (MMRM)		
n	33	37
LS mean (SE)	-0.02 (2.02)	1.16 (1.91)
95% CI of LS mean	(-4.05, 4.02)	(-2.65, 4.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.18 (-4.39, 6.75)
Week 16 (MMRM)		
n	32	36
LS mean (SE)	94.37 (1.78)	96.13 (1.68)
95% CI of LS mean	(90.81, 97.93)	(92.76, 99.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.76 (-3.16, 6.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 16 (MMRM)		
n	31	36
LS mean (SE)	-0.95 (1.73)	2.42 (1.62)
95% CI of LS mean	(-4.41, 2.51)	(-0.83, 5.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.37 (-1.41, 8.15)
Week 24 (MMRM)		
n	34	36
LS mean (SE)	93.13 (2.25)	95.28 (2.17)
95% CI of LS mean	(88.63, 97.63)	(90.95, 99.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.14 (-4.11, 8.40)
Absolute Change at Week 24 (MMRM)		
n	33	35
LS mean (SE)	-1.89 (1.72)	1.33 (1.67)
95% CI of LS mean	(-5.33, 1.55)	(-2.00, 4.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.22 (-1.60, 8.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52		
n	33	35
Mean (SD)	96.97 (7.99)	96.83 (6.36)
Absolute Change at Week 52		
n	32	34
Mean (SD)	1.74 (8.52)	1.31 (13.33)
Week 52 (MMRM)		
n	32	35
LS mean (SE)	96.73 (1.23)	96.33 (1.19)
95% CI of LS mean	(94.28, 99.19)	(93.96, 98.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.40 (-3.84, 3.04)
Absolute Change at Week 52 (MMRM)		
n	31	34
LS mean (SE)	0.67 (2.03)	2.41 (1.94)
95% CI of LS mean	(-3.39, 4.73)	(-1.46, 6.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.74 (-3.89, 7.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change through Week 52 (MMRM)		
n	33	38
LS mean (SE)	-0.72 (1.36)	2.05 (1.29)
95% CI of LS mean	(-3.44, 1.99)	(-0.54, 4.64)
P-value within Treatment	0.5956	0.1179
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.78 (-1.01, 6.56)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1478
Hedges' G (SE)		0.35 (0.24)
Hedges' 95% CI		(-0.13, 0.82)
Hedges' P-value		0.1470

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	92.36 (15.10)	94.28 (11.78)
Week 8 (MMRM)		
n	243	237
LS mean (SE)	92.13 (0.91)	93.86 (0.93)
95% CI of LS mean	(90.34, 93.93)	(92.04, 95.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.73 (-0.83, 4.29)
Absolute Change at Week 8 (MMRM)		
n	237	234
LS mean (SE)	0.16 (0.69)	-0.40 (0.70)
95% CI of LS mean	(-1.20, 1.53)	(-1.78, 0.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.57 (-2.51, 1.37)
Week 16 (MMRM)		
n	241	232
LS mean (SE)	92.42 (0.96)	92.65 (0.98)
95% CI of LS mean	(90.52, 94.32)	(90.72, 94.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.23 (-2.48, 2.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 16 (MMRM)		
n	235	229
LS mean (SE)	0.42 (0.78)	-1.57 (0.79)
95% CI of LS mean	(-1.12, 1.96)	(-3.12, -0.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.99 (-4.18, 0.20)
Week 24 (MMRM)		
n	240	229
LS mean (SE)	92.38 (1.01)	92.11 (1.03)
95% CI of LS mean	(90.39, 94.36)	(90.09, 94.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.27 (-3.11, 2.57)
Absolute Change at Week 24 (MMRM)		
n	234	227
LS mean (SE)	0.29 (0.82)	-2.11 (0.83)
95% CI of LS mean	(-1.31, 1.90)	(-3.74, -0.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.41 (-4.70, -0.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52		
n	244	230
Mean (SD)	92.40 (15.56)	92.85 (14.21)
Absolute Change at Week 52		
n	238	227
Mean (SD)	0.30 (13.81)	-1.40 (11.13)
Week 52 (MMRM)		
n	237	224
LS mean (SE)	92.45 (0.96)	92.91 (0.98)
95% CI of LS mean	(90.56, 94.34)	(90.98, 94.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.46 (-2.25, 3.16)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	0.32 (0.82)	-1.28 (0.84)
95% CI of LS mean	(-1.30, 1.93)	(-2.93, 0.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.60 (-3.91, 0.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	0.34 (0.64)	-1.65 (0.64)
95% CI of LS mean	(-0.91, 1.59)	(-2.92, -0.39)
P-value within Treatment	0.5891	0.0106
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.00 (-3.78, -0.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0280
Hedges' G (SE)		-0.20 (0.09)
Hedges' 95% CI		(-0.39, -0.02)
Hedges' P-value		0.0282

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	78	71
Mean (SD)	90.67 (17.83)	94.37 (12.72)
Week 8 (MMRM)		
n	79	69
LS mean (SE)	91.57 (1.65)	94.51 (1.77)
95% CI of LS mean	(88.31, 94.83)	(91.02, 98.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.94 (-1.85, 7.73)
Absolute Change at Week 8 (MMRM)		
n	77	68
LS mean (SE)	0.82 (1.26)	0.13 (1.35)
95% CI of LS mean	(-1.68, 3.32)	(-2.53, 2.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.70 (-4.36, 2.97)
Week 16 (MMRM)		
n	77	67
LS mean (SE)	91.50 (1.65)	92.56 (1.77)
95% CI of LS mean	(88.24, 94.76)	(89.06, 96.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.05 (-3.74, 5.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 16 (MMRM)		
n	75	66
LS mean (SE)	1.08 (1.11)	-1.79 (1.19)
95% CI of LS mean	(-1.12, 3.28)	(-4.13, 0.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.87 (-6.10, 0.36)
Week 24 (MMRM)		
n	79	63
LS mean (SE)	90.73 (1.77)	92.70 (1.93)
95% CI of LS mean	(87.23, 94.22)	(88.89, 96.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.98 (-3.21, 7.16)
Absolute Change at Week 24 (MMRM)		
n	77	63
LS mean (SE)	-0.04 (1.40)	-1.63 (1.54)
95% CI of LS mean	(-2.82, 2.74)	(-4.67, 1.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.59 (-5.71, 2.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52		
n	78	67
Mean (SD)	92.31 (15.33)	93.03 (14.32)
Absolute Change at Week 52		
n	76	66
Mean (SD)	1.68 (11.30)	-1.52 (9.53)
Week 52 (MMRM)		
n	77	64
LS mean (SE)	92.29 (1.70)	92.85 (1.84)
95% CI of LS mean	(88.92, 95.66)	(89.21, 96.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.57 (-4.40, 5.54)
Absolute Change at Week 52 (MMRM)		
n	75	63
LS mean (SE)	1.62 (1.21)	-1.45 (1.31)
95% CI of LS mean	(-0.78, 4.01)	(-4.04, 1.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.07 (-6.61, 0.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change through Week 52 (MMRM)		
n	77	66
LS mean (SE)	0.89 (1.06)	-1.62 (1.14)
95% CI of LS mean	(-1.21, 2.98)	(-3.88, 0.64)
P-value within Treatment	0.4041	0.1577
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.51 (-5.60, 0.58)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1111
Hedges' G (SE)		-0.27 (0.17)
Hedges' 95% CI		(-0.60, 0.06)
Hedges' P-value		0.1112

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	197	207
Mean (SD)	93.46 (13.03)	94.12 (11.75)
Week 8 (MMRM)		
n	198	205
LS mean (SE)	92.91 (0.96)	93.92 (0.94)
95% CI of LS mean	(91.03, 94.79)	(92.07, 95.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.00 (-1.63, 3.64)
Absolute Change at Week 8 (MMRM)		
n	193	203
LS mean (SE)	-0.07 (0.77)	-0.28 (0.76)
95% CI of LS mean	(-1.59, 1.45)	(-1.76, 1.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.21 (-2.34, 1.92)
Week 16 (MMRM)		
n	196	201
LS mean (SE)	93.10 (1.04)	93.37 (1.02)
95% CI of LS mean	(91.07, 95.14)	(91.36, 95.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.26 (-2.59, 3.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 16 (MMRM)		
n	191	199
LS mean (SE)	-0.01 (0.90)	-0.84 (0.89)
95% CI of LS mean	(-1.79, 1.77)	(-2.58, 0.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.83 (-3.32, 1.66)
Week 24 (MMRM)		
n	195	202
LS mean (SE)	93.18 (1.09)	92.53 (1.07)
95% CI of LS mean	(91.03, 95.33)	(90.42, 94.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.65 (-3.66, 2.36)
Absolute Change at Week 24 (MMRM)		
n	190	199
LS mean (SE)	0.11 (0.88)	-1.69 (0.86)
95% CI of LS mean	(-1.62, 1.85)	(-3.38, 0.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.80 (-4.23, 0.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52		
n	194	196
Mean (SD)	93.24 (14.71)	93.65 (13.03)
Absolute Change at Week 52		
n	189	193
Mean (SD)	0.12 (14.08)	-0.66 (11.69)
Week 52 (MMRM)		
n	192	195
LS mean (SE)	93.12 (1.00)	93.63 (0.98)
95% CI of LS mean	(91.16, 95.08)	(91.70, 95.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.51 (-2.24, 3.27)
Absolute Change at Week 52 (MMRM)		
n	187	192
LS mean (SE)	-0.08 (0.95)	-0.60 (0.94)
95% CI of LS mean	(-1.95, 1.78)	(-2.44, 1.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.52 (-3.14, 2.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change through Week 52 (MMRM)		
n	193	202
LS mean (SE)	0.01 (0.70)	-1.04 (0.68)
95% CI of LS mean	(-1.37, 1.38)	(-2.39, 0.30)
P-value within Treatment	0.9919	0.1278
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.05 (-2.98, 0.87)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2834
Hedges' G (SE)		-0.11 (0.10)
Hedges' 95% CI		(-0.31, 0.09)
Hedges' P-value		0.2835

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	140	146
Mean (SD)	93.25 (13.90)	94.52 (12.19)
Week 8 (MMRM)		
n	134	143
LS mean (SE)	93.21 (1.06)	94.88 (1.03)
95% CI of LS mean	(91.12, 95.30)	(92.86, 96.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.67 (-1.26, 4.59)
Absolute Change at Week 8 (MMRM)		
n	130	141
LS mean (SE)	0.01 (0.85)	0.49 (0.82)
95% CI of LS mean	(-1.67, 1.69)	(-1.12, 2.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.48 (-1.86, 2.82)
Week 16 (MMRM)		
n	130	139
LS mean (SE)	93.89 (1.10)	93.17 (1.06)
95% CI of LS mean	(91.73, 96.05)	(91.08, 95.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.72 (-3.74, 2.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 16 (MMRM)		
n	126	137
LS mean (SE)	0.89 (0.84)	-1.20 (0.81)
95% CI of LS mean	(-0.76, 2.55)	(-2.79, 0.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.09 (-4.40, 0.22)
Week 24 (MMRM)		
n	133	140
LS mean (SE)	93.19 (1.20)	93.25 (1.16)
95% CI of LS mean	(90.83, 95.55)	(90.96, 95.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-3.24, 3.37)
Absolute Change at Week 24 (MMRM)		
n	129	137
LS mean (SE)	0.08 (0.91)	-1.14 (0.88)
95% CI of LS mean	(-1.71, 1.87)	(-2.87, 0.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.22 (-3.72, 1.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52		
n	139	143
Mean (SD)	93.05 (14.61)	94.09 (12.36)
Absolute Change at Week 52		
n	135	140
Mean (SD)	0.08 (14.14)	-0.32 (10.99)
Week 52 (MMRM)		
n	132	139
LS mean (SE)	93.07 (1.19)	94.00 (1.15)
95% CI of LS mean	(90.73, 95.41)	(91.72, 96.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (-2.35, 4.20)
Absolute Change at Week 52 (MMRM)		
n	128	136
LS mean (SE)	-0.13 (1.14)	-0.35 (1.11)
95% CI of LS mean	(-2.38, 2.13)	(-2.53, 1.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-3.37, 2.92)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change through Week 52 (MMRM)		
n	130	139
LS mean (SE)	0.28 (0.80)	-0.90 (0.77)
95% CI of LS mean	(-1.29, 1.85)	(-2.41, 0.62)
P-value within Treatment	0.7232	0.2459
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.18 (-3.37, 1.02)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2911
Hedges' G (SE)		-0.13 (0.12)
Hedges' 95% CI		(-0.37, 0.11)
Hedges' P-value		0.2891

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	142	134
Mean (SD)	92.29 (15.03)	93.91 (11.72)
Week 8 (MMRM)		
n	143	131
LS mean (SE)	92.07 (1.28)	92.96 (1.33)
95% CI of LS mean	(89.56, 94.58)	(90.33, 95.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.88 (-2.77, 4.54)
Absolute Change at Week 8 (MMRM)		
n	140	130
LS mean (SE)	0.43 (1.02)	-1.01 (1.05)
95% CI of LS mean	(-1.58, 2.43)	(-3.09, 1.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.44 (-4.34, 1.46)
Week 16 (MMRM)		
n	143	129
LS mean (SE)	91.60 (1.37)	92.97 (1.43)
95% CI of LS mean	(88.91, 94.30)	(90.15, 95.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.37 (-2.55, 5.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 16 (MMRM)		
n	140	128
LS mean (SE)	-0.21 (1.17)	-1.05 (1.22)
95% CI of LS mean	(-2.51, 2.09)	(-3.45, 1.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.84 (-4.18, 2.50)
Week 24 (MMRM)		
n	141	125
LS mean (SE)	91.95 (1.43)	91.65 (1.51)
95% CI of LS mean	(89.13, 94.76)	(88.68, 94.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-4.40, 3.80)
Absolute Change at Week 24 (MMRM)		
n	138	125
LS mean (SE)	0.08 (1.19)	-2.37 (1.25)
95% CI of LS mean	(-2.27, 2.43)	(-4.83, 0.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.45 (-5.86, 0.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52		
n	138	122
Mean (SD)	92.83 (15.30)	92.53 (14.74)
Absolute Change at Week 52		
n	135	121
Mean (SD)	0.86 (12.42)	-1.88 (11.95)
Week 52 (MMRM)		
n	137	120
LS mean (SE)	92.78 (1.27)	92.48 (1.34)
95% CI of LS mean	(90.28, 95.28)	(89.84, 95.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-3.95, 3.36)
Absolute Change at Week 52 (MMRM)		
n	134	119
LS mean (SE)	0.85 (1.04)	-1.61 (1.10)
95% CI of LS mean	(-1.21, 2.90)	(-3.77, 0.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.45 (-5.45, 0.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change through Week 52 (MMRM)		
n	140	129
LS mean (SE)	0.24 (0.87)	-1.68 (0.91)
95% CI of LS mean	(-1.48, 1.96)	(-3.47, 0.12)
P-value within Treatment	0.7844	0.0670
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.91 (-4.42, 0.59)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1328
Hedges' G (SE)		-0.18 (0.12)
Hedges' 95% CI		(-0.42, 0.06)
Hedges' P-value		0.1313

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	102	111
Mean (SD)	91.07 (15.16)	93.59 (13.28)
Week 8 (MMRM)		
n	98	112
LS mean (SE)	89.49 (1.40)	94.69 (1.31)
95% CI of LS mean	(86.73, 92.25)	(92.11, 97.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.20 (1.42, 8.98)
Absolute Change at Week 8 (MMRM)		
n	97	109
LS mean (SE)	-1.03 (1.07)	1.09 (1.00)
95% CI of LS mean	(-3.14, 1.07)	(-0.90, 3.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.12 (-0.77, 5.01)
Week 16 (MMRM)		
n	96	108
LS mean (SE)	89.81 (1.46)	93.52 (1.37)
95% CI of LS mean	(86.93, 92.68)	(90.82, 96.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.71 (-0.24, 7.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 16 (MMRM)		
n	95	105
LS mean (SE)	-0.79 (1.04)	-0.10 (0.99)
95% CI of LS mean	(-2.84, 1.25)	(-2.05, 1.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.69 (-2.14, 3.51)
Week 24 (MMRM)		
n	98	108
LS mean (SE)	90.92 (1.65)	92.94 (1.55)
95% CI of LS mean	(87.67, 94.16)	(89.87, 96.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.02 (-2.45, 6.49)
Absolute Change at Week 24 (MMRM)		
n	97	106
LS mean (SE)	0.42 (1.02)	-0.74 (0.98)
95% CI of LS mean	(-1.60, 2.44)	(-2.67, 1.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.16 (-3.95, 1.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52		
n	101	104
Mean (SD)	90.98 (16.61)	93.38 (13.00)
Absolute Change at Week 52		
n	100	101
Mean (SD)	0.33 (12.58)	-0.22 (12.07)
Week 52 (MMRM)		
n	97	104
LS mean (SE)	91.03 (1.50)	93.39 (1.43)
95% CI of LS mean	(88.07, 93.99)	(90.57, 96.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.36 (-1.74, 6.45)
Absolute Change at Week 52 (MMRM)		
n	96	101
LS mean (SE)	0.55 (1.25)	-0.12 (1.21)
95% CI of LS mean	(-1.92, 3.02)	(-2.52, 2.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.67 (-4.11, 2.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change through Week 52 (MMRM)		
n	98	107
LS mean (SE)	0.06 (0.83)	-0.32 (0.79)
95% CI of LS mean	(-1.58, 1.70)	(-1.89, 1.24)
P-value within Treatment	0.9449	0.6847
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-2.65, 1.89)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7414
Hedges' G (SE)		-0.05 (0.14)
Hedges' 95% CI		(-0.32, 0.23)
Hedges' P-value		0.7410

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	180	169
Mean (SD)	93.73 (14.00)	94.64 (11.01)
Week 8 (MMRM)		
n	179	162
LS mean (SE)	94.25 (1.01)	93.58 (1.06)
95% CI of LS mean	(92.26, 96.24)	(91.49, 95.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.67 (-3.56, 2.22)
Absolute Change at Week 8 (MMRM)		
n	173	162
LS mean (SE)	0.83 (0.84)	-0.98 (0.87)
95% CI of LS mean	(-0.83, 2.48)	(-2.69, 0.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.81 (-4.19, 0.58)
Week 16 (MMRM)		
n	177	160
LS mean (SE)	94.20 (1.08)	92.88 (1.14)
95% CI of LS mean	(92.07, 96.33)	(90.64, 95.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.31 (-4.41, 1.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	171	160
LS mean (SE)	0.81 (0.98)	-1.68 (1.01)
95% CI of LS mean	(-1.12, 2.74)	(-3.68, 0.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.50 (-5.27, 0.28)
Week 24 (MMRM)		
n	176	157
LS mean (SE)	93.37 (1.11)	92.26 (1.17)
95% CI of LS mean	(91.18, 95.55)	(89.95, 94.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.11 (-4.29, 2.07)
Absolute Change at Week 24 (MMRM)		
n	170	156
LS mean (SE)	-0.25 (1.03)	-2.30 (1.07)
95% CI of LS mean	(-2.27, 1.78)	(-4.41, -0.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.05 (-4.98, 0.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52		
n	176	161
Mean (SD)	94.07 (13.80)	93.37 (13.85)
Absolute Change at Week 52		
n	170	160
Mean (SD)	0.56 (13.72)	-1.56 (11.04)
Week 52 (MMRM)		
n	172	155
LS mean (SE)	93.93 (1.04)	93.46 (1.09)
95% CI of LS mean	(91.89, 95.97)	(91.31, 95.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-3.43, 2.50)
Absolute Change at Week 52 (MMRM)		
n	166	154
LS mean (SE)	0.24 (0.97)	-1.18 (1.01)
95% CI of LS mean	(-1.67, 2.15)	(-3.16, 0.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.43 (-4.18, 1.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	172	161
LS mean (SE)	0.27 (0.80)	-1.72 (0.83)
95% CI of LS mean	(-1.30, 1.84)	(-3.35, -0.10)
P-value within Treatment	0.7355	0.0377
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.99 (-4.25, 0.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0838
Hedges' G (SE)		-0.19 (0.11)
Hedges' 95% CI		(-0.41, 0.03)
Hedges' P-value		0.0840

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	164	152
Mean (SD)	80.28 (17.20)	83.16 (17.96)
Week 8 (MMRM)		
n	161	153
LS mean (SE)	81.07 (1.40)	83.41 (1.43)
95% CI of LS mean	(78.32, 83.82)	(80.59, 86.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.34 (-1.60, 6.28)
Absolute Change at Week 8 (MMRM)		
n	158	151
LS mean (SE)	1.02 (0.86)	0.44 (0.88)
95% CI of LS mean	(-0.67, 2.71)	(-1.30, 2.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.58 (-3.01, 1.84)
Week 16 (MMRM)		
n	158	149
LS mean (SE)	80.83 (1.39)	81.89 (1.43)
95% CI of LS mean	(78.09, 83.58)	(79.07, 84.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.06 (-2.88, 4.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 16 (MMRM)		
n	155	147
LS mean (SE)	0.91 (0.92)	-1.03 (0.94)
95% CI of LS mean	(-0.90, 2.72)	(-2.89, 0.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.94 (-4.54, 0.66)
Week 24 (MMRM)		
n	155	147
LS mean (SE)	81.06 (1.39)	82.28 (1.42)
95% CI of LS mean	(78.33, 83.79)	(79.48, 85.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.22 (-2.69, 5.14)
Absolute Change at Week 24 (MMRM)		
n	152	145
LS mean (SE)	0.97 (0.97)	-0.67 (0.99)
95% CI of LS mean	(-0.93, 2.87)	(-2.62, 1.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.64 (-4.36, 1.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52		
n	159	145
Mean (SD)	80.42 (18.58)	81.79 (19.25)
Absolute Change at Week 52		
n	156	143
Mean (SD)	0.09 (15.24)	-0.79 (14.73)
Week 52 (MMRM)		
n	155	144
LS mean (SE)	80.16 (1.49)	81.89 (1.54)
95% CI of LS mean	(77.22, 83.10)	(78.86, 84.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.73 (-2.49, 5.96)
Absolute Change at Week 52 (MMRM)		
n	152	142
LS mean (SE)	-0.02 (1.22)	-0.99 (1.25)
95% CI of LS mean	(-2.41, 2.38)	(-3.46, 1.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.98 (-4.42, 2.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	0.62 (0.86)	-0.90 (0.88)
95% CI of LS mean	(-1.06, 2.30)	(-2.63, 0.83)
P-value within Treatment	0.4688	0.3069
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.52 (-3.93, 0.89)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2166
Hedges' G (SE)		-0.14 (0.11)
Hedges' 95% CI		(-0.37, 0.08)
Hedges' P-value		0.2168

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	115	123
Mean (SD)	83.81 (14.95)	80.20 (17.65)
Week 8 (MMRM)		
n	115	121
LS mean (SE)	84.23 (1.48)	81.98 (1.44)
95% CI of LS mean	(81.32, 87.14)	(79.14, 84.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.25 (-6.33, 1.83)
Absolute Change at Week 8 (MMRM)		
n	112	120
LS mean (SE)	0.13 (1.11)	1.91 (1.07)
95% CI of LS mean	(-2.05, 2.32)	(-0.20, 4.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.78 (-1.27, 4.83)
Week 16 (MMRM)		
n	115	119
LS mean (SE)	84.98 (1.50)	80.10 (1.46)
95% CI of LS mean	(82.03, 87.93)	(77.22, 82.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.88 (-9.02, -0.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 16 (MMRM)		
n	111	118
LS mean (SE)	1.17 (1.16)	0.08 (1.12)
95% CI of LS mean	(-1.11, 3.45)	(-2.13, 2.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.09 (-4.28, 2.09)
Week 24 (MMRM)		
n	118	118
LS mean (SE)	82.86 (1.60)	79.51 (1.57)
95% CI of LS mean	(79.72, 86.01)	(76.42, 82.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.35 (-7.78, 1.08)
Absolute Change at Week 24 (MMRM)		
n	114	117
LS mean (SE)	-1.15 (1.25)	-0.54 (1.23)
95% CI of LS mean	(-3.62, 1.32)	(-2.96, 1.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.61 (-2.86, 4.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52		
n	115	116
Mean (SD)	83.37 (14.52)	81.75 (17.25)
Absolute Change at Week 52		
n	111	114
Mean (SD)	-0.87 (12.27)	1.43 (14.36)
Week 52 (MMRM)		
n	114	115
LS mean (SE)	83.35 (1.50)	81.45 (1.47)
95% CI of LS mean	(80.40, 86.29)	(78.55, 84.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.90 (-6.04, 2.25)
Absolute Change at Week 52 (MMRM)		
n	110	113
LS mean (SE)	-0.79 (1.27)	1.44 (1.24)
95% CI of LS mean	(-3.28, 1.71)	(-1.00, 3.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.23 (-1.27, 5.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change through Week 52 (MMRM)		
n	114	120
LS mean (SE)	-0.26 (1.05)	0.33 (1.02)
95% CI of LS mean	(-2.33, 1.82)	(-1.69, 2.34)
P-value within Treatment	0.8086	0.7510
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-2.32, 3.49)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6939
Hedges' G (SE)		0.05 (0.13)
Hedges' 95% CI		(-0.21, 0.31)
Hedges' P-value		0.6930

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	37	40
Mean (SD)	84.91 (15.02)	79.60 (18.72)
Week 8 (MMRM)		
n	34	37
LS mean (SE)	86.62 (2.53)	81.21 (2.41)
95% CI of LS mean	(81.58, 91.67)	(76.41, 86.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.41 (-12.44, 1.61)
Absolute Change at Week 8 (MMRM)		
n	33	37
LS mean (SE)	1.82 (1.77)	1.37 (1.67)
95% CI of LS mean	(-1.71, 5.35)	(-1.96, 4.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.45 (-5.34, 4.45)
Week 16 (MMRM)		
n	32	36
LS mean (SE)	85.09 (2.97)	80.69 (2.81)
95% CI of LS mean	(79.17, 91.01)	(75.09, 86.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.40 (-12.60, 3.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 16 (MMRM)		
n	31	36
LS mean (SE)	0.45 (2.30)	0.98 (2.15)
95% CI of LS mean	(-4.13, 5.04)	(-3.32, 5.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.53 (-5.79, 6.84)
Week 24 (MMRM)		
n	34	36
LS mean (SE)	86.25 (2.69)	81.23 (2.56)
95% CI of LS mean	(80.87, 91.63)	(76.11, 86.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.03 (-12.50, 2.45)
Absolute Change at Week 24 (MMRM)		
n	33	35
LS mean (SE)	1.69 (2.02)	1.39 (1.92)
95% CI of LS mean	(-2.34, 5.73)	(-2.45, 5.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-5.90, 5.30)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52		
n	33	35
Mean (SD)	84.07 (16.83)	84.07 (16.47)
Absolute Change at Week 52		
n	32	34
Mean (SD)	-1.46 (17.06)	1.86 (18.41)
Week 52 (MMRM)		
n	32	35
LS mean (SE)	83.21 (3.01)	82.19 (2.86)
95% CI of LS mean	(77.19, 89.22)	(76.47, 87.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.02 (-9.36, 7.33)
Absolute Change at Week 52 (MMRM)		
n	31	34
LS mean (SE)	-2.19 (3.24)	2.16 (3.07)
95% CI of LS mean	(-8.65, 4.27)	(-3.98, 8.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.35 (-4.59, 13.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change through Week 52 (MMRM)		
n	33	38
LS mean (SE)	-0.01 (2.29)	1.51 (2.16)
95% CI of LS mean	(-4.59, 4.56)	(-2.81, 5.83)
P-value within Treatment	0.9949	0.4874
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.53 (-4.80, 7.85)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6314
Hedges' G (SE)		0.11 (0.24)
Hedges' 95% CI		(-0.36, 0.58)
Hedges' P-value		0.6303

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	81.35 (16.49)	82.11 (17.61)
Week 8 (MMRM)		
n	242	237
LS mean (SE)	81.65 (1.11)	83.10 (1.12)
95% CI of LS mean	(79.47, 83.84)	(80.89, 85.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.45 (-1.66, 4.55)
Absolute Change at Week 8 (MMRM)		
n	237	234
LS mean (SE)	0.52 (0.74)	0.94 (0.74)
95% CI of LS mean	(-0.93, 1.97)	(-0.52, 2.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.41 (-1.65, 2.47)
Week 16 (MMRM)		
n	241	232
LS mean (SE)	82.05 (1.10)	81.25 (1.12)
95% CI of LS mean	(79.89, 84.22)	(79.05, 83.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.80 (-3.89, 2.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 16 (MMRM)		
n	235	229
LS mean (SE)	1.09 (0.76)	-0.85 (0.76)
95% CI of LS mean	(-0.39, 2.58)	(-2.35, 0.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.94 (-4.06, 0.17)
Week 24 (MMRM)		
n	239	229
LS mean (SE)	81.01 (1.14)	81.13 (1.16)
95% CI of LS mean	(78.78, 83.25)	(78.86, 83.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-3.08, 3.32)
Absolute Change at Week 24 (MMRM)		
n	233	227
LS mean (SE)	-0.16 (0.84)	-1.00 (0.85)
95% CI of LS mean	(-1.80, 1.49)	(-2.66, 0.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.85 (-3.18, 1.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52		
n	244	230
Mean (SD)	81.37 (17.01)	81.57 (18.53)
Absolute Change at Week 52		
n	238	227
Mean (SD)	-0.21 (13.57)	0.12 (13.99)
Week 52 (MMRM)		
n	237	224
LS mean (SE)	81.10 (1.15)	81.76 (1.17)
95% CI of LS mean	(78.85, 83.35)	(79.46, 84.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.66 (-2.56, 3.88)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	-0.16 (0.91)	-0.27 (0.92)
95% CI of LS mean	(-1.94, 1.62)	(-2.08, 1.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-2.65, 2.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	0.26 (0.69)	-0.71 (0.70)
95% CI of LS mean	(-1.10, 1.62)	(-2.08, 0.67)
P-value within Treatment	0.7079	0.3126
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.97 (-2.90, 0.97)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3268
Hedges' G (SE)		-0.09 (0.09)
Hedges' 95% CI		(-0.27, 0.09)
Hedges' P-value		0.3265

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	78	71
Mean (SD)	82.08 (17.29)	82.98 (16.84)
Week 8 (MMRM)		
n	79	69
LS mean (SE)	84.00 (1.95)	83.90 (2.09)
95% CI of LS mean	(80.14, 87.86)	(79.77, 88.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-5.77, 5.57)
Absolute Change at Week 8 (MMRM)		
n	77	68
LS mean (SE)	2.16 (1.29)	1.24 (1.37)
95% CI of LS mean	(-0.39, 4.71)	(-1.47, 3.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.92 (-4.65, 2.82)
Week 16 (MMRM)		
n	77	67
LS mean (SE)	81.22 (2.02)	82.89 (2.17)
95% CI of LS mean	(77.22, 85.22)	(78.60, 87.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.67 (-4.21, 7.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 16 (MMRM)		
n	75	66
LS mean (SE)	-0.34 (1.27)	0.29 (1.35)
95% CI of LS mean	(-2.84, 2.17)	(-2.38, 2.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-3.05, 4.31)
Week 24 (MMRM)		
n	78	63
LS mean (SE)	79.74 (2.01)	82.51 (2.18)
95% CI of LS mean	(75.76, 83.72)	(78.19, 86.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.77 (-3.11, 8.65)
Absolute Change at Week 24 (MMRM)		
n	76	63
LS mean (SE)	-2.32 (1.42)	-0.10 (1.55)
95% CI of LS mean	(-5.14, 0.50)	(-3.16, 2.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.22 (-1.95, 6.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52		
n	78	67
Mean (SD)	81.01 (17.43)	84.91 (17.30)
Absolute Change at Week 52		
n	76	66
Mean (SD)	-1.18 (12.67)	2.18 (16.46)
Week 52 (MMRM)		
n	77	64
LS mean (SE)	81.05 (1.98)	84.21 (2.14)
95% CI of LS mean	(77.15, 84.96)	(79.98, 88.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.15 (-2.61, 8.92)
Absolute Change at Week 52 (MMRM)		
n	75	63
LS mean (SE)	-1.18 (1.64)	1.60 (1.77)
95% CI of LS mean	(-4.42, 2.06)	(-1.91, 5.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.78 (-2.00, 7.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change through Week 52 (MMRM)		
n	77	66
LS mean (SE)	-1.28 (1.21)	0.60 (1.30)
95% CI of LS mean	(-3.67, 1.11)	(-1.98, 3.17)
P-value within Treatment	0.2916	0.6462
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.88 (-1.65, 5.40)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2940
Hedges' G (SE)		0.18 (0.17)
Hedges' 95% CI		(-0.15, 0.51)
Hedges' P-value		0.2932

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	197	207
Mean (SD)	81.59 (15.84)	81.32 (18.09)
Week 8 (MMRM)		
n	197	205
LS mean (SE)	81.67 (1.20)	82.47 (1.18)
95% CI of LS mean	(79.31, 84.03)	(80.16, 84.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.80 (-2.50, 4.10)
Absolute Change at Week 8 (MMRM)		
n	193	203
LS mean (SE)	0.05 (0.80)	1.02 (0.78)
95% CI of LS mean	(-1.53, 1.62)	(-0.52, 2.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-1.23, 3.18)
Week 16 (MMRM)		
n	196	201
LS mean (SE)	83.03 (1.19)	80.57 (1.17)
95% CI of LS mean	(80.69, 85.37)	(78.27, 82.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.46 (-5.74, 0.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 16 (MMRM)		
n	191	199
LS mean (SE)	1.56 (0.87)	-0.83 (0.85)
95% CI of LS mean	(-0.14, 3.27)	(-2.50, 0.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.39 (-4.78, 0.00)
Week 24 (MMRM)		
n	195	202
LS mean (SE)	82.55 (1.22)	80.65 (1.20)
95% CI of LS mean	(80.15, 84.96)	(78.29, 83.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.90 (-5.27, 1.47)
Absolute Change at Week 24 (MMRM)		
n	190	199
LS mean (SE)	1.04 (0.90)	-0.81 (0.88)
95% CI of LS mean	(-0.74, 2.82)	(-2.55, 0.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.85 (-4.34, 0.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52		
n	194	196
Mean (SD)	81.87 (16.88)	80.82 (18.54)
Absolute Change at Week 52		
n	189	193
Mean (SD)	-0.02 (14.61)	-0.32 (13.99)
Week 52 (MMRM)		
n	192	195
LS mean (SE)	81.62 (1.26)	80.93 (1.25)
95% CI of LS mean	(79.13, 84.11)	(78.48, 83.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.69 (-4.18, 2.81)
Absolute Change at Week 52 (MMRM)		
n	187	192
LS mean (SE)	0.01 (1.04)	-0.42 (1.02)
95% CI of LS mean	(-2.03, 2.06)	(-2.43, 1.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.43 (-3.30, 2.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change through Week 52 (MMRM)		
n	193	202
LS mean (SE)	0.87 (0.79)	-0.69 (0.77)
95% CI of LS mean	(-0.67, 2.42)	(-2.20, 0.83)
P-value within Treatment	0.2676	0.3730
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.56 (-3.72, 0.60)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1574
Hedges' G (SE)		-0.14 (0.10)
Hedges' 95% CI		(-0.34, 0.06)
Hedges' P-value		0.1577

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	140	146
Mean (SD)	83.05 (16.23)	83.89 (18.23)
Week 8 (MMRM)		
n	134	143
LS mean (SE)	83.50 (1.43)	84.80 (1.38)
95% CI of LS mean	(80.69, 86.31)	(82.08, 87.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.30 (-2.64, 5.23)
Absolute Change at Week 8 (MMRM)		
n	130	141
LS mean (SE)	0.92 (0.99)	1.08 (0.96)
95% CI of LS mean	(-1.04, 2.87)	(-0.80, 2.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-2.56, 2.89)
Week 16 (MMRM)		
n	130	139
LS mean (SE)	83.83 (1.43)	84.06 (1.39)
95% CI of LS mean	(81.01, 86.65)	(81.33, 86.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.24 (-3.71, 4.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 16 (MMRM)		
n	126	137
LS mean (SE)	1.60 (1.02)	0.45 (0.98)
95% CI of LS mean	(-0.40, 3.60)	(-1.48, 2.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.15 (-3.94, 1.63)
Week 24 (MMRM)		
n	132	140
LS mean (SE)	83.65 (1.41)	84.30 (1.37)
95% CI of LS mean	(80.87, 86.42)	(81.61, 86.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.65 (-3.24, 4.54)
Absolute Change at Week 24 (MMRM)		
n	128	137
LS mean (SE)	1.14 (1.00)	0.67 (0.96)
95% CI of LS mean	(-0.83, 3.10)	(-1.23, 2.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-3.21, 2.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52		
n	139	143
Mean (SD)	83.87 (14.98)	83.96 (18.25)
Absolute Change at Week 52		
n	135	140
Mean (SD)	0.78 (12.13)	0.77 (14.18)
Week 52 (MMRM)		
n	132	139
LS mean (SE)	83.63 (1.47)	84.08 (1.42)
95% CI of LS mean	(80.75, 86.52)	(81.28, 86.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-3.60, 4.49)
Absolute Change at Week 52 (MMRM)		
n	128	136
LS mean (SE)	0.94 (1.19)	0.59 (1.15)
95% CI of LS mean	(-1.40, 3.27)	(-1.67, 2.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.35 (-3.61, 2.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change through Week 52 (MMRM)		
n	130	139
LS mean (SE)	1.23 (0.90)	0.57 (0.87)
95% CI of LS mean	(-0.55, 3.01)	(-1.15, 2.29)
P-value within Treatment	0.1765	0.5166
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.66 (-3.15, 1.83)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6033
Hedges' G (SE)		-0.06 (0.12)
Hedges' 95% CI		(-0.30, 0.18)
Hedges' P-value		0.6013

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	142	134
Mean (SD)	80.60 (16.38)	79.43 (17.00)
Week 8 (MMRM)		
n	142	131
LS mean (SE)	81.39 (1.45)	80.48 (1.51)
95% CI of LS mean	(78.53, 84.25)	(77.50, 83.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.92 (-5.07, 3.24)
Absolute Change at Week 8 (MMRM)		
n	140	130
LS mean (SE)	0.58 (0.95)	0.87 (0.99)
95% CI of LS mean	(-1.30, 2.45)	(-1.07, 2.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.30 (-2.42, 3.01)
Week 16 (MMRM)		
n	143	129
LS mean (SE)	81.43 (1.46)	77.79 (1.53)
95% CI of LS mean	(78.55, 84.31)	(74.79, 80.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.64 (-7.82, 0.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 16 (MMRM)		
n	140	128
LS mean (SE)	0.64 (1.03)	-1.82 (1.07)
95% CI of LS mean	(-1.38, 2.66)	(-3.93, 0.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.46 (-5.39, 0.47)
Week 24 (MMRM)		
n	141	125
LS mean (SE)	80.12 (1.53)	77.43 (1.61)
95% CI of LS mean	(77.11, 83.13)	(74.27, 80.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.69 (-7.08, 1.70)
Absolute Change at Week 24 (MMRM)		
n	138	125
LS mean (SE)	-0.74 (1.17)	-2.23 (1.22)
95% CI of LS mean	(-3.03, 1.56)	(-4.63, 0.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.49 (-4.83, 1.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52		
n	138	122
Mean (SD)	79.49 (18.57)	79.47 (18.05)
Absolute Change at Week 52		
n	135	121
Mean (SD)	-1.49 (15.61)	-0.15 (15.15)
Week 52 (MMRM)		
n	137	120
LS mean (SE)	79.54 (1.54)	79.02 (1.62)
95% CI of LS mean	(76.51, 82.57)	(75.83, 82.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.52 (-4.95, 3.90)
Absolute Change at Week 52 (MMRM)		
n	134	119
LS mean (SE)	-1.35 (1.31)	-0.61 (1.37)
95% CI of LS mean	(-3.93, 1.22)	(-3.31, 2.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.75 (-3.00, 4.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change through Week 52 (MMRM)		
n	140	129
LS mean (SE)	-0.49 (0.97)	-1.55 (1.01)
95% CI of LS mean	(-2.40, 1.43)	(-3.55, 0.44)
P-value within Treatment	0.6180	0.1267
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.07 (-3.85, 1.71)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4505
Hedges' G (SE)		-0.09 (0.12)
Hedges' 95% CI		(-0.33, 0.15)
Hedges' P-value		0.4482

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	102	111
Mean (SD)	81.23 (17.43)	83.31 (17.95)
Week 8 (MMRM)		
n	98	112
LS mean (SE)	80.47 (1.87)	84.08 (1.75)
95% CI of LS mean	(76.78, 84.16)	(80.62, 87.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.60 (-1.46, 8.66)
Absolute Change at Week 8 (MMRM)		
n	97	109
LS mean (SE)	-0.27 (1.15)	0.84 (1.08)
95% CI of LS mean	(-2.53, 1.99)	(-1.29, 2.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.11 (-2.00, 4.22)
Week 16 (MMRM)		
n	96	108
LS mean (SE)	81.86 (1.71)	83.57 (1.61)
95% CI of LS mean	(78.48, 85.23)	(80.41, 86.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.72 (-2.92, 6.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 16 (MMRM)		
n	95	105
LS mean (SE)	1.21 (1.13)	0.39 (1.07)
95% CI of LS mean	(-1.02, 3.44)	(-1.73, 2.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.82 (-3.90, 2.25)
Week 24 (MMRM)		
n	97	108
LS mean (SE)	79.82 (1.72)	84.58 (1.62)
95% CI of LS mean	(76.42, 83.22)	(81.39, 87.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.76 (0.09, 9.43)
Absolute Change at Week 24 (MMRM)		
n	96	106
LS mean (SE)	-0.84 (1.13)	1.29 (1.07)
95% CI of LS mean	(-3.06, 1.39)	(-0.83, 3.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.13 (-0.95, 5.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52		
n	101	104
Mean (SD)	79.88 (17.62)	83.04 (17.79)
Absolute Change at Week 52		
n	100	101
Mean (SD)	-1.24 (13.72)	0.29 (13.72)
Week 52 (MMRM)		
n	97	104
LS mean (SE)	79.56 (1.78)	83.30 (1.69)
95% CI of LS mean	(76.05, 83.07)	(79.97, 86.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.74 (-1.10, 8.58)
Absolute Change at Week 52 (MMRM)		
n	96	101
LS mean (SE)	-1.12 (1.40)	0.16 (1.36)
95% CI of LS mean	(-3.89, 1.65)	(-2.52, 2.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.27 (-2.58, 5.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change through Week 52 (MMRM)		
n	98	107
LS mean (SE)	-0.25 (1.03)	0.61 (0.98)
95% CI of LS mean	(-2.27, 1.77)	(-1.32, 2.54)
P-value within Treatment	0.8090	0.5330
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.86 (-1.94, 3.66)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5458
Hedges' G (SE)		0.08 (0.14)
Hedges' 95% CI		(-0.19, 0.36)
Hedges' P-value		0.5452

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	180	169
Mean (SD)	82.15 (15.71)	80.73 (17.61)
Week 8 (MMRM)		
n	178	162
LS mean (SE)	83.26 (1.19)	82.06 (1.25)
95% CI of LS mean	(80.92, 85.61)	(79.60, 84.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.20 (-4.61, 2.20)
Absolute Change at Week 8 (MMRM)		
n	173	162
LS mean (SE)	1.20 (0.86)	1.21 (0.88)
95% CI of LS mean	(-0.48, 2.88)	(-0.53, 2.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-2.42, 2.43)
Week 16 (MMRM)		
n	177	160
LS mean (SE)	82.79 (1.28)	79.62 (1.34)
95% CI of LS mean	(80.27, 85.30)	(76.98, 82.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.17 (-6.82, 0.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	171	160
LS mean (SE)	0.94 (0.93)	-1.21 (0.96)
95% CI of LS mean	(-0.89, 2.77)	(-3.11, 0.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.15 (-4.79, 0.48)
Week 24 (MMRM)		
n	176	157
LS mean (SE)	82.69 (1.31)	78.87 (1.38)
95% CI of LS mean	(80.12, 85.27)	(76.16, 81.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.82 (-7.56, -0.08)
Absolute Change at Week 24 (MMRM)		
n	170	156
LS mean (SE)	0.60 (1.03)	-1.96 (1.07)
95% CI of LS mean	(-1.42, 2.62)	(-4.06, 0.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.56 (-5.47, 0.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52		
n	176	161
Mean (SD)	82.73 (16.56)	81.15 (18.58)
Absolute Change at Week 52		
n	170	160
Mean (SD)	0.16 (14.18)	0.38 (15.20)
Week 52 (MMRM)		
n	172	155
LS mean (SE)	82.38 (1.33)	80.79 (1.40)
95% CI of LS mean	(79.75, 85.00)	(78.03, 83.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.59 (-5.39, 2.22)
Absolute Change at Week 52 (MMRM)		
n	166	154
LS mean (SE)	0.14 (1.13)	-0.01 (1.18)
95% CI of LS mean	(-2.10, 2.37)	(-2.32, 2.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-3.36, 3.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	172	161
LS mean (SE)	0.56 (0.87)	-1.06 (0.90)
95% CI of LS mean	(-1.15, 2.26)	(-2.83, 0.70)
P-value within Treatment	0.5204	0.2375
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.62 (-4.08, 0.84)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1957
Hedges' G (SE)		-0.14 (0.11)
Hedges' 95% CI		(-0.36, 0.07)
Hedges' P-value		0.1956

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	163	152
Mean (SD)	67.96 (19.85)	70.94 (19.26)
Week 8 (MMRM)		
n	161	153
LS mean (SE)	67.64 (1.59)	69.57 (1.63)
95% CI of LS mean	(64.50, 70.77)	(66.35, 72.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.93 (-2.56, 6.43)
Absolute Change at Week 8 (MMRM)		
n	158	151
LS mean (SE)	0.12 (1.18)	-1.20 (1.20)
95% CI of LS mean	(-2.19, 2.44)	(-3.57, 1.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.32 (-4.64, 1.99)
Week 16 (MMRM)		
n	158	148
LS mean (SE)	67.87 (1.58)	69.43 (1.63)
95% CI of LS mean	(64.75, 70.98)	(66.22, 72.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.57 (-2.91, 6.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 16 (MMRM)		
n	155	146
LS mean (SE)	0.65 (1.22)	-1.35 (1.26)
95% CI of LS mean	(-1.75, 3.06)	(-3.83, 1.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.01 (-5.46, 1.45)
Week 24 (MMRM)		
n	156	147
LS mean (SE)	65.89 (1.72)	69.76 (1.77)
95% CI of LS mean	(62.51, 69.27)	(66.29, 73.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.88 (-0.97, 8.73)
Absolute Change at Week 24 (MMRM)		
n	153	145
LS mean (SE)	-1.38 (1.35)	-0.92 (1.38)
95% CI of LS mean	(-4.03, 1.27)	(-3.63, 1.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.47 (-3.33, 4.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52		
n	159	145
Mean (SD)	69.95 (19.83)	71.19 (19.27)
Absolute Change at Week 52		
n	156	143
Mean (SD)	2.21 (16.62)	0.51 (14.32)
Week 52 (MMRM)		
n	155	144
LS mean (SE)	69.64 (1.54)	70.80 (1.59)
95% CI of LS mean	(66.60, 72.68)	(67.67, 73.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.16 (-3.21, 5.53)
Absolute Change at Week 52 (MMRM)		
n	152	142
LS mean (SE)	2.15 (1.26)	0.16 (1.30)
95% CI of LS mean	(-0.33, 4.63)	(-2.39, 2.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.99 (-5.55, 1.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	0.47 (1.03)	-0.70 (1.06)
95% CI of LS mean	(-1.55, 2.50)	(-2.78, 1.38)
P-value within Treatment	0.6458	0.5074
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.18 (-4.08, 1.73)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4268
Hedges' G (SE)		-0.09 (0.11)
Hedges' 95% CI		(-0.32, 0.13)
Hedges' P-value		0.4266

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	103	109
Mean (SD)	76.91 (18.19)	75.94 (20.65)
Week 8 (MMRM)		
n	106	107
LS mean (SE)	77.07 (1.77)	75.12 (1.75)
95% CI of LS mean	(73.58, 80.56)	(71.67, 78.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.95 (-6.88, 2.98)
Absolute Change at Week 8 (MMRM)		
n	103	106
LS mean (SE)	-0.27 (1.42)	-0.77 (1.39)
95% CI of LS mean	(-3.06, 2.52)	(-3.51, 1.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.50 (-4.43, 3.43)
Week 16 (MMRM)		
n	105	106
LS mean (SE)	76.11 (1.79)	75.47 (1.77)
95% CI of LS mean	(72.57, 79.64)	(71.98, 78.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.63 (-5.63, 4.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 16 (MMRM)		
n	102	105
LS mean (SE)	-0.95 (1.50)	-0.50 (1.47)
95% CI of LS mean	(-3.91, 2.01)	(-3.40, 2.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-3.71, 4.61)
Week 24 (MMRM)		
n	106	104
LS mean (SE)	75.39 (1.84)	75.33 (1.84)
95% CI of LS mean	(71.76, 79.03)	(71.71, 78.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-5.21, 5.09)
Absolute Change at Week 24 (MMRM)		
n	103	104
LS mean (SE)	-1.67 (1.55)	-0.79 (1.53)
95% CI of LS mean	(-4.73, 1.38)	(-3.81, 2.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.89 (-3.42, 5.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52		
n	104	102
Mean (SD)	80.02 (17.34)	76.36 (19.70)
Absolute Change at Week 52		
n	101	101
Mean (SD)	2.64 (14.75)	0.00 (15.63)
Week 52 (MMRM)		
n	104	101
LS mean (SE)	79.68 (1.83)	76.29 (1.83)
95% CI of LS mean	(76.08, 83.29)	(72.68, 79.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.39 (-8.51, 1.73)
Absolute Change at Week 52 (MMRM)		
n	101	100
LS mean (SE)	2.45 (1.53)	0.21 (1.53)
95% CI of LS mean	(-0.57, 5.47)	(-2.80, 3.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.24 (-6.51, 2.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change through Week 52 (MMRM)		
n	103	106
LS mean (SE)	-0.06 (1.24)	-0.36 (1.22)
95% CI of LS mean	(-2.51, 2.39)	(-2.77, 2.05)
P-value within Treatment	0.9624	0.7698
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-3.75, 3.15)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8641
Hedges' G (SE)		-0.02 (0.14)
Hedges' 95% CI		(-0.30, 0.25)
Hedges' P-value		0.8636

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	24	26
Mean (SD)	82.87 (17.02)	76.92 (25.71)
Week 8 (MMRM)		
n	24	23
LS mean (SE)	81.59 (4.61)	78.52 (4.57)
95% CI of LS mean	(72.28, 90.90)	(69.29, 87.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.07 (-16.37, 10.23)
Absolute Change at Week 8 (MMRM)		
n	24	23
LS mean (SE)	-0.96 (4.05)	0.78 (4.02)
95% CI of LS mean	(-9.17, 7.25)	(-7.37, 8.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.73 (-9.93, 13.40)
Week 16 (MMRM)		
n	22	23
LS mean (SE)	81.84 (4.67)	78.03 (4.57)
95% CI of LS mean	(72.36, 91.31)	(68.75, 87.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.81 (-17.25, 9.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 16 (MMRM)		
n	22	23
LS mean (SE)	-0.32 (4.07)	-1.00 (3.99)
95% CI of LS mean	(-8.65, 8.00)	(-9.14, 7.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.67 (-12.43, 11.09)
Week 24 (MMRM)		
n	22	22
LS mean (SE)	81.26 (3.59)	80.83 (3.54)
95% CI of LS mean	(73.93, 88.60)	(73.60, 88.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.43 (-10.96, 10.10)
Absolute Change at Week 24 (MMRM)		
n	22	22
LS mean (SE)	-1.19 (3.50)	-0.06 (3.47)
95% CI of LS mean	(-8.38, 6.00)	(-7.17, 7.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.13 (-9.11, 11.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52		
n	22	21
Mean (SD)	87.88 (15.30)	77.78 (19.25)
Absolute Change at Week 52		
n	22	21
Mean (SD)	4.55 (10.66)	-5.82 (18.80)
Week 52 (MMRM)		
n	22	21
LS mean (SE)	85.15 (3.99)	77.26 (4.08)
95% CI of LS mean	(76.98, 93.32)	(68.95, 85.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.89 (-19.75, 3.96)
Absolute Change at Week 52 (MMRM)		
n	22	21
LS mean (SE)	4.72 (3.14)	-5.10 (3.28)
95% CI of LS mean	(-1.68, 11.11)	(-11.76, 1.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.81 (-19.22, -0.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change through Week 52 (MMRM)		
n	22	24
LS mean (SE)	1.07 (2.77)	-2.05 (2.76)
95% CI of LS mean	(-4.60, 6.74)	(-7.68, 3.58)
P-value within Treatment	0.7022	0.4626
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.12 (-11.28, 5.04)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4410
Hedges' G (SE)		-0.23 (0.29)
Hedges' 95% CI		(-0.82, 0.36)
Hedges' P-value		0.4311

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	70.34 (19.53)	72.34 (19.36)
Week 8 (MMRM)		
n	243	237
LS mean (SE)	70.27 (1.24)	71.37 (1.25)
95% CI of LS mean	(67.84, 72.69)	(68.91, 73.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.10 (-2.36, 4.56)
Absolute Change at Week 8 (MMRM)		
n	237	234
LS mean (SE)	0.06 (0.92)	-1.03 (0.93)
95% CI of LS mean	(-1.75, 1.87)	(-2.85, 0.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.09 (-3.66, 1.48)
Week 16 (MMRM)		
n	241	231
LS mean (SE)	69.94 (1.23)	71.39 (1.25)
95% CI of LS mean	(67.52, 72.36)	(68.93, 73.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.45 (-2.01, 4.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 16 (MMRM)		
n	235	228
LS mean (SE)	-0.04 (0.97)	-0.99 (0.99)
95% CI of LS mean	(-1.95, 1.87)	(-2.93, 0.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.95 (-3.68, 1.77)
Week 24 (MMRM)		
n	240	229
LS mean (SE)	68.49 (1.34)	71.33 (1.37)
95% CI of LS mean	(65.86, 71.13)	(68.64, 74.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.84 (-0.93, 6.61)
Absolute Change at Week 24 (MMRM)		
n	234	227
LS mean (SE)	-1.53 (1.07)	-0.95 (1.08)
95% CI of LS mean	(-3.63, 0.56)	(-3.08, 1.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.59 (-2.41, 3.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52		
n	244	230
Mean (SD)	72.72 (19.32)	73.00 (19.68)
Absolute Change at Week 52		
n	238	227
Mean (SD)	2.19 (16.23)	1.05 (14.32)
Week 52 (MMRM)		
n	237	224
LS mean (SE)	72.52 (1.24)	72.84 (1.27)
95% CI of LS mean	(70.08, 74.95)	(70.36, 75.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.33 (-3.16, 3.81)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	2.28 (1.01)	0.67 (1.03)
95% CI of LS mean	(0.30, 4.27)	(-1.35, 2.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.62 (-4.45, 1.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	0.24 (0.82)	-0.43 (0.83)
95% CI of LS mean	(-1.38, 1.85)	(-2.07, 1.21)
P-value within Treatment	0.7743	0.6103
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.66 (-2.97, 1.64)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5732
Hedges' G (SE)		-0.05 (0.09)
Hedges' 95% CI		(-0.23, 0.13)
Hedges' P-value		0.5728

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	77	70
Mean (SD)	69.55 (20.97)	74.76 (20.80)
Week 8 (MMRM)		
n	78	67
LS mean (SE)	70.83 (2.26)	72.24 (2.43)
95% CI of LS mean	(66.36, 75.29)	(67.44, 77.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.41 (-5.16, 7.98)
Absolute Change at Week 8 (MMRM)		
n	76	66
LS mean (SE)	0.45 (1.55)	-1.99 (1.65)
95% CI of LS mean	(-2.61, 3.50)	(-5.26, 1.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.43 (-6.93, 2.06)
Week 16 (MMRM)		
n	77	66
LS mean (SE)	69.23 (2.41)	69.44 (2.59)
95% CI of LS mean	(64.46, 73.99)	(64.31, 74.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.21 (-6.80, 7.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 16 (MMRM)		
n	75	65
LS mean (SE)	-0.77 (1.90)	-4.96 (2.04)
95% CI of LS mean	(-4.53, 2.99)	(-9.00, -0.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.19 (-9.72, 1.34)
Week 24 (MMRM)		
n	78	62
LS mean (SE)	67.77 (2.42)	72.97 (2.64)
95% CI of LS mean	(62.98, 72.55)	(67.75, 78.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.20 (-1.89, 12.30)
Absolute Change at Week 24 (MMRM)		
n	76	62
LS mean (SE)	-2.41 (1.67)	-1.44 (1.82)
95% CI of LS mean	(-5.70, 0.89)	(-5.05, 2.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-3.93, 5.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52		
n	77	66
Mean (SD)	72.29 (20.28)	73.40 (22.21)
Absolute Change at Week 52		
n	75	65
Mean (SD)	2.52 (12.99)	-1.37 (16.26)
Week 52 (MMRM)		
n	76	63
LS mean (SE)	72.49 (2.42)	72.35 (2.63)
95% CI of LS mean	(67.70, 77.28)	(67.16, 77.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-7.22, 6.95)
Absolute Change at Week 52 (MMRM)		
n	74	62
LS mean (SE)	2.27 (1.69)	-1.84 (1.84)
95% CI of LS mean	(-1.08, 5.62)	(-5.49, 1.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.12 (-9.08, 0.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change through Week 52 (MMRM)		
n	76	65
LS mean (SE)	-0.30 (1.37)	-2.75 (1.48)
95% CI of LS mean	(-3.01, 2.41)	(-5.67, 0.18)
P-value within Treatment	0.8266	0.0652
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.45 (-6.45, 1.55)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2284
Hedges' G (SE)		-0.20 (0.17)
Hedges' 95% CI		(-0.54, 0.13)
Hedges' P-value		0.2278

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	187	194
Mean (SD)	71.95 (19.01)	72.02 (19.85)
Week 8 (MMRM)		
n	189	193
LS mean (SE)	71.61 (1.41)	71.75 (1.39)
95% CI of LS mean	(68.84, 74.38)	(69.01, 74.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-3.76, 4.04)
Absolute Change at Week 8 (MMRM)		
n	185	191
LS mean (SE)	-0.22 (1.11)	-0.68 (1.09)
95% CI of LS mean	(-2.40, 1.96)	(-2.82, 1.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.46 (-3.51, 2.60)
Week 16 (MMRM)		
n	186	188
LS mean (SE)	71.94 (1.36)	72.82 (1.35)
95% CI of LS mean	(69.26, 74.62)	(70.17, 75.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.88 (-2.90, 4.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 16 (MMRM)		
n	182	186
LS mean (SE)	0.34 (1.08)	0.39 (1.06)
95% CI of LS mean	(-1.78, 2.46)	(-1.70, 2.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.06 (-2.92, 3.04)
Week 24 (MMRM)		
n	184	189
LS mean (SE)	70.49 (1.49)	71.80 (1.47)
95% CI of LS mean	(67.56, 73.42)	(68.91, 74.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.31 (-2.81, 5.43)
Absolute Change at Week 24 (MMRM)		
n	180	187
LS mean (SE)	-1.11 (1.25)	-0.64 (1.23)
95% CI of LS mean	(-3.57, 1.34)	(-3.05, 1.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.47 (-2.97, 3.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52		
n	185	183
Mean (SD)	74.59 (19.00)	73.28 (18.71)
Absolute Change at Week 52		
n	181	181
Mean (SD)	2.58 (16.82)	1.07 (14.33)
Week 52 (MMRM)		
n	183	182
LS mean (SE)	74.13 (1.36)	73.38 (1.35)
95% CI of LS mean	(71.45, 76.81)	(70.71, 76.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.75 (-4.53, 3.03)
Absolute Change at Week 52 (MMRM)		
n	179	180
LS mean (SE)	2.29 (1.18)	0.95 (1.17)
95% CI of LS mean	(-0.03, 4.61)	(-1.35, 3.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.35 (-4.61, 1.92)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change through Week 52 (MMRM)		
n	183	189
LS mean (SE)	0.51 (0.96)	0.23 (0.94)
95% CI of LS mean	(-1.38, 2.39)	(-1.62, 2.09)
P-value within Treatment	0.5978	0.8049
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.27 (-2.92, 2.37)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8396
Hedges' G (SE)		-0.02 (0.10)
Hedges' 95% CI		(-0.22, 0.18)
Hedges' P-value		0.8395

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	133	141
Mean (SD)	72.10 (19.52)	74.59 (20.33)
Week 8 (MMRM)		
n	130	139
LS mean (SE)	70.16 (1.70)	74.35 (1.65)
95% CI of LS mean	(66.81, 73.52)	(71.10, 77.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.18 (-0.51, 8.88)
Absolute Change at Week 8 (MMRM)		
n	127	137
LS mean (SE)	-1.45 (1.27)	-0.81 (1.22)
95% CI of LS mean	(-3.95, 1.05)	(-3.21, 1.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.64 (-2.85, 4.13)
Week 16 (MMRM)		
n	126	134
LS mean (SE)	71.57 (1.67)	73.97 (1.61)
95% CI of LS mean	(68.29, 74.86)	(70.79, 77.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.39 (-2.20, 6.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 16 (MMRM)		
n	123	132
LS mean (SE)	0.23 (1.37)	-1.13 (1.32)
95% CI of LS mean	(-2.46, 2.93)	(-3.74, 1.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.37 (-5.13, 2.40)
Week 24 (MMRM)		
n	127	134
LS mean (SE)	70.57 (1.76)	75.64 (1.71)
95% CI of LS mean	(67.10, 74.05)	(72.27, 79.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.06 (0.20, 9.93)
Absolute Change at Week 24 (MMRM)		
n	124	132
LS mean (SE)	-0.70 (1.49)	0.65 (1.44)
95% CI of LS mean	(-3.63, 2.24)	(-2.19, 3.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.35 (-2.75, 5.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52		
n	132	137
Mean (SD)	73.57 (19.20)	75.02 (20.02)
Absolute Change at Week 52		
n	129	135
Mean (SD)	1.38 (17.01)	0.95 (14.69)
Week 52 (MMRM)		
n	126	133
LS mean (SE)	72.86 (1.74)	75.25 (1.69)
95% CI of LS mean	(69.43, 76.28)	(71.92, 78.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.39 (-2.41, 7.20)
Absolute Change at Week 52 (MMRM)		
n	123	131
LS mean (SE)	1.29 (1.45)	0.31 (1.41)
95% CI of LS mean	(-1.57, 4.16)	(-2.46, 3.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.98 (-4.98, 3.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change through Week 52 (MMRM)		
n	125	134
LS mean (SE)	0.28 (1.21)	-0.06 (1.17)
95% CI of LS mean	(-2.10, 2.66)	(-2.35, 2.24)
P-value within Treatment	0.8183	0.9613
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-3.66, 2.99)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8432
Hedges' G (SE)		-0.02 (0.12)
Hedges' 95% CI		(-0.27, 0.22)
Hedges' P-value		0.8423

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	136	125
Mean (SD)	70.83 (19.78)	70.76 (19.63)
Week 8 (MMRM)		
n	137	121
LS mean (SE)	72.79 (1.68)	68.76 (1.78)
95% CI of LS mean	(69.47, 76.10)	(65.26, 72.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.02 (-8.88, 0.84)
Absolute Change at Week 8 (MMRM)		
n	134	120
LS mean (SE)	1.44 (1.29)	-1.45 (1.36)
95% CI of LS mean	(-1.11, 3.99)	(-4.13, 1.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.89 (-6.61, 0.83)
Week 16 (MMRM)		
n	137	120
LS mean (SE)	71.00 (1.71)	69.36 (1.81)
95% CI of LS mean	(67.64, 74.37)	(65.79, 72.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.64 (-6.58, 3.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 16 (MMRM)		
n	134	119
LS mean (SE)	-0.13 (1.32)	-1.03 (1.40)
95% CI of LS mean	(-2.74, 2.47)	(-3.78, 1.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.90 (-4.70, 2.91)
Week 24 (MMRM)		
n	135	117
LS mean (SE)	69.12 (1.82)	67.73 (1.94)
95% CI of LS mean	(65.54, 72.70)	(63.91, 71.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.40 (-6.66, 3.86)
Absolute Change at Week 24 (MMRM)		
n	132	117
LS mean (SE)	-2.16 (1.39)	-2.76 (1.47)
95% CI of LS mean	(-4.90, 0.58)	(-5.66, 0.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.60 (-4.60, 3.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52		
n	134	114
Mean (SD)	74.38 (19.76)	71.44 (19.10)
Absolute Change at Week 52		
n	131	113
Mean (SD)	3.39 (14.58)	-0.10 (15.03)
Week 52 (MMRM)		
n	133	112
LS mean (SE)	74.64 (1.64)	70.43 (1.75)
95% CI of LS mean	(71.42, 77.86)	(66.98, 73.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.21 (-8.96, 0.53)
Absolute Change at Week 52 (MMRM)		
n	130	111
LS mean (SE)	3.28 (1.30)	-0.03 (1.40)
95% CI of LS mean	(0.71, 5.85)	(-2.79, 2.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.31 (-7.09, 0.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change through Week 52 (MMRM)		
n	134	120
LS mean (SE)	0.33 (1.04)	-1.27 (1.10)
95% CI of LS mean	(-1.72, 2.38)	(-3.45, 0.90)
P-value within Treatment	0.7526	0.2490
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.60 (-4.61, 1.41)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2949
Hedges' G (SE)		-0.13 (0.13)
Hedges' 95% CI		(-0.38, 0.11)
Hedges' P-value		0.2924

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	99	108
Mean (SD)	73.96 (19.52)	76.34 (19.52)
Week 8 (MMRM)		
n	96	109
LS mean (SE)	70.36 (1.89)	75.06 (1.76)
95% CI of LS mean	(66.64, 74.08)	(71.58, 78.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.70 (-0.40, 9.80)
Absolute Change at Week 8 (MMRM)		
n	95	106
LS mean (SE)	-2.96 (1.39)	-1.51 (1.31)
95% CI of LS mean	(-5.70, -0.23)	(-4.10, 1.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.45 (-2.32, 5.22)
Week 16 (MMRM)		
n	94	105
LS mean (SE)	73.18 (1.78)	77.01 (1.68)
95% CI of LS mean	(69.66, 76.69)	(73.71, 80.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.84 (-1.00, 8.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 16 (MMRM)		
n	93	102
LS mean (SE)	-0.24 (1.28)	0.50 (1.22)
95% CI of LS mean	(-2.76, 2.28)	(-1.90, 2.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.73 (-2.75, 4.22)
Week 24 (MMRM)		
n	95	105
LS mean (SE)	69.69 (1.92)	76.89 (1.80)
95% CI of LS mean	(65.91, 73.46)	(73.33, 80.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.20 (2.01, 12.40)
Absolute Change at Week 24 (MMRM)		
n	94	103
LS mean (SE)	-3.54 (1.44)	0.52 (1.37)
95% CI of LS mean	(-6.38, -0.70)	(-2.18, 3.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.06 (0.14, 7.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52		
n	98	101
Mean (SD)	75.06 (19.02)	75.36 (19.73)
Absolute Change at Week 52		
n	97	98
Mean (SD)	1.15 (14.39)	-0.68 (14.69)
Week 52 (MMRM)		
n	94	101
LS mean (SE)	74.43 (1.91)	75.58 (1.81)
95% CI of LS mean	(70.68, 78.19)	(72.01, 79.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.14 (-4.05, 6.33)
Absolute Change at Week 52 (MMRM)		
n	93	98
LS mean (SE)	1.04 (1.50)	-0.66 (1.45)
95% CI of LS mean	(-1.93, 4.00)	(-3.53, 2.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.70 (-5.83, 2.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change through Week 52 (MMRM)		
n	95	104
LS mean (SE)	-0.91 (1.15)	0.12 (1.09)
95% CI of LS mean	(-3.17, 1.35)	(-2.04, 2.27)
P-value within Treatment	0.4268	0.9138
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.03 (-2.10, 4.16)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5166
Hedges' G (SE)		0.09 (0.14)
Hedges' 95% CI		(-0.19, 0.37)
Hedges' P-value		0.5161

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	170	158
Mean (SD)	70.00 (19.60)	70.36 (20.12)
Week 8 (MMRM)		
n	171	151
LS mean (SE)	71.97 (1.53)	69.53 (1.63)
95% CI of LS mean	(68.95, 74.99)	(66.32, 72.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.44 (-6.85, 1.96)
Absolute Change at Week 8 (MMRM)		
n	166	151
LS mean (SE)	1.69 (1.17)	-0.76 (1.23)
95% CI of LS mean	(-0.61, 4.00)	(-3.17, 1.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.46 (-5.80, 0.89)
Week 16 (MMRM)		
n	169	149
LS mean (SE)	70.00 (1.56)	68.27 (1.65)
95% CI of LS mean	(66.93, 73.06)	(65.02, 71.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.73 (-6.20, 2.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	149
LS mean (SE)	0.15 (1.31)	-2.10 (1.37)
95% CI of LS mean	(-2.42, 2.72)	(-4.80, 0.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.25 (-5.98, 1.48)
Week 24 (MMRM)		
n	167	146
LS mean (SE)	69.66 (1.67)	68.54 (1.78)
95% CI of LS mean	(66.37, 72.95)	(65.03, 72.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.13 (-5.94, 3.68)
Absolute Change at Week 24 (MMRM)		
n	162	146
LS mean (SE)	-0.29 (1.37)	-1.88 (1.44)
95% CI of LS mean	(-2.99, 2.41)	(-4.71, 0.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.58 (-5.50, 2.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52		
n	168	150
Mean (SD)	73.35 (19.72)	72.07 (19.55)
Absolute Change at Week 52		
n	163	150
Mean (SD)	3.14 (16.63)	1.22 (14.91)
Week 52 (MMRM)		
n	165	144
LS mean (SE)	73.17 (1.53)	71.19 (1.63)
95% CI of LS mean	(70.16, 76.19)	(67.98, 74.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.98 (-6.39, 2.43)
Absolute Change at Week 52 (MMRM)		
n	160	144
LS mean (SE)	3.00 (1.27)	0.74 (1.33)
95% CI of LS mean	(0.51, 5.50)	(-1.88, 3.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.26 (-5.88, 1.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	150
LS mean (SE)	0.95 (1.06)	-1.08 (1.11)
95% CI of LS mean	(-1.14, 3.04)	(-3.27, 1.11)
P-value within Treatment	0.3700	0.3331
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.03 (-5.07, 1.00)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1884
Hedges' G (SE)		-0.15 (0.11)
Hedges' 95% CI		(-0.37, 0.07)
Hedges' P-value		0.1880

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	164	152
Mean (SD)	77.35 (21.33)	80.92 (19.11)
Week 8 (MMRM)		
n	161	153
LS mean (SE)	74.79 (1.60)	79.51 (1.64)
95% CI of LS mean	(71.63, 77.94)	(76.27, 82.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.72 (0.20, 9.24)
Absolute Change at Week 8 (MMRM)		
n	158	151
LS mean (SE)	-2.49 (1.33)	-1.23 (1.36)
95% CI of LS mean	(-5.12, 0.13)	(-3.91, 1.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.27 (-2.49, 5.02)
Week 16 (MMRM)		
n	158	149
LS mean (SE)	76.29 (1.64)	80.12 (1.69)
95% CI of LS mean	(73.06, 79.53)	(76.80, 83.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.83 (-0.81, 8.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 16 (MMRM)		
n	155	147
LS mean (SE)	-0.73 (1.29)	-0.43 (1.33)
95% CI of LS mean	(-3.28, 1.81)	(-3.04, 2.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.31 (-3.34, 3.95)
Week 24 (MMRM)		
n	155	147
LS mean (SE)	75.53 (1.68)	79.22 (1.73)
95% CI of LS mean	(72.22, 78.84)	(75.82, 82.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.69 (-1.06, 8.43)
Absolute Change at Week 24 (MMRM)		
n	152	145
LS mean (SE)	-1.78 (1.29)	-1.34 (1.32)
95% CI of LS mean	(-4.31, 0.75)	(-3.93, 1.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.44 (-3.18, 4.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52		
n	159	145
Mean (SD)	76.54 (21.91)	81.79 (18.22)
Absolute Change at Week 52		
n	156	143
Mean (SD)	-0.11 (16.86)	0.99 (12.52)
Week 52 (MMRM)		
n	155	144
LS mean (SE)	77.11 (1.53)	81.36 (1.58)
95% CI of LS mean	(74.10, 80.12)	(78.26, 84.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.25 (-0.08, 8.58)
Absolute Change at Week 52 (MMRM)		
n	152	142
LS mean (SE)	-0.17 (1.21)	0.80 (1.25)
95% CI of LS mean	(-2.55, 2.21)	(-1.66, 3.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-2.45, 4.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	-0.89 (0.98)	-0.32 (1.00)
95% CI of LS mean	(-2.81, 1.02)	(-2.29, 1.64)
P-value within Treatment	0.3595	0.7463
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.57 (-2.18, 3.32)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6834
Hedges' G (SE)		0.05 (0.11)
Hedges' 95% CI		(-0.18, 0.27)
Hedges' P-value		0.6831

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	115	123
Mean (SD)	85.34 (18.08)	85.56 (17.85)
Week 8 (MMRM)		
n	115	121
LS mean (SE)	87.61 (1.76)	85.45 (1.72)
95% CI of LS mean	(84.14, 91.08)	(82.06, 88.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.16 (-7.02, 2.70)
Absolute Change at Week 8 (MMRM)		
n	112	120
LS mean (SE)	1.96 (1.33)	-0.31 (1.29)
95% CI of LS mean	(-0.67, 4.59)	(-2.85, 2.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.27 (-5.94, 1.39)
Week 16 (MMRM)		
n	115	119
LS mean (SE)	88.24 (1.66)	85.62 (1.62)
95% CI of LS mean	(84.97, 91.50)	(82.42, 88.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.62 (-7.21, 1.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 16 (MMRM)		
n	111	118
LS mean (SE)	2.79 (1.25)	-0.11 (1.22)
95% CI of LS mean	(0.32, 5.27)	(-2.50, 2.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.90 (-6.35, 0.55)
Week 24 (MMRM)		
n	118	118
LS mean (SE)	87.19 (1.71)	85.66 (1.68)
95% CI of LS mean	(83.82, 90.56)	(82.35, 88.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.53 (-6.27, 3.22)
Absolute Change at Week 24 (MMRM)		
n	114	117
LS mean (SE)	1.56 (1.27)	0.17 (1.24)
95% CI of LS mean	(-0.94, 4.05)	(-2.27, 2.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.38 (-4.89, 2.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52		
n	115	116
Mean (SD)	88.00 (16.14)	87.52 (18.06)
Absolute Change at Week 52		
n	111	114
Mean (SD)	2.47 (15.93)	1.66 (12.41)
Week 52 (MMRM)		
n	114	115
LS mean (SE)	87.76 (1.63)	87.02 (1.61)
95% CI of LS mean	(84.54, 90.99)	(83.85, 90.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.74 (-5.28, 3.79)
Absolute Change at Week 52 (MMRM)		
n	110	113
LS mean (SE)	2.34 (1.39)	1.30 (1.36)
95% CI of LS mean	(-0.40, 5.09)	(-1.38, 3.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.04 (-4.89, 2.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change through Week 52 (MMRM)		
n	114	120
LS mean (SE)	2.23 (1.11)	0.46 (1.08)
95% CI of LS mean	(0.05, 4.41)	(-1.67, 2.58)
P-value within Treatment	0.0453	0.6725
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.77 (-4.83, 1.28)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2542
Hedges' G (SE)		-0.15 (0.13)
Hedges' 95% CI		(-0.41, 0.11)
Hedges' P-value		0.2534

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	37	40
Mean (SD)	86.99 (16.74)	88.27 (13.46)
Week 8 (MMRM)		
n	34	37
LS mean (SE)	90.74 (2.72)	87.71 (2.59)
95% CI of LS mean	(85.32, 96.17)	(82.54, 92.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.03 (-10.57, 4.50)
Absolute Change at Week 8 (MMRM)		
n	33	37
LS mean (SE)	3.85 (2.35)	-1.31 (2.22)
95% CI of LS mean	(-0.84, 8.53)	(-5.74, 3.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.16 (-11.65, 1.34)
Week 16 (MMRM)		
n	32	36
LS mean (SE)	89.94 (2.65)	88.69 (2.50)
95% CI of LS mean	(84.65, 95.24)	(83.69, 93.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.25 (-8.58, 6.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 16 (MMRM)		
n	31	36
LS mean (SE)	3.33 (2.38)	0.09 (2.23)
95% CI of LS mean	(-1.41, 8.07)	(-4.36, 4.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.24 (-9.78, 3.31)
Week 24 (MMRM)		
n	34	36
LS mean (SE)	88.72 (2.49)	90.91 (2.38)
95% CI of LS mean	(83.74, 93.70)	(86.16, 95.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.18 (-4.74, 9.11)
Absolute Change at Week 24 (MMRM)		
n	33	35
LS mean (SE)	2.11 (2.32)	2.57 (2.21)
95% CI of LS mean	(-2.54, 6.75)	(-1.86, 6.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.46 (-6.00, 6.92)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52		
n	33	35
Mean (SD)	94.02 (9.61)	92.58 (12.50)
Absolute Change at Week 52		
n	32	34
Mean (SD)	7.10 (17.84)	2.06 (13.53)
Week 52 (MMRM)		
n	32	35
LS mean (SE)	93.00 (2.18)	91.42 (2.07)
95% CI of LS mean	(88.64, 97.36)	(87.27, 95.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.58 (-7.65, 4.49)
Absolute Change at Week 52 (MMRM)		
n	31	34
LS mean (SE)	5.68 (2.77)	2.04 (2.62)
95% CI of LS mean	(0.13, 11.23)	(-3.22, 7.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.64 (-11.33, 4.04)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change through Week 52 (MMRM)		
n	33	38
LS mean (SE)	3.70 (2.30)	1.56 (2.17)
95% CI of LS mean	(-0.90, 8.31)	(-2.78, 5.91)
P-value within Treatment	0.1126	0.4739
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.14 (-8.51, 4.23)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5042
Hedges' G (SE)		-0.16 (0.24)
Hedges' 95% CI		(-0.63, 0.31)
Hedges' P-value		0.5019

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	79.71 (20.65)	81.92 (19.20)
Week 8 (MMRM)		
n	242	237
LS mean (SE)	78.66 (1.31)	81.21 (1.32)
95% CI of LS mean	(76.09, 81.24)	(78.61, 83.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.55 (-1.12, 6.21)
Absolute Change at Week 8 (MMRM)		
n	237	234
LS mean (SE)	-1.30 (1.03)	-0.72 (1.04)
95% CI of LS mean	(-3.33, 0.72)	(-2.76, 1.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-2.29, 3.45)
Week 16 (MMRM)		
n	241	232
LS mean (SE)	80.08 (1.30)	81.52 (1.32)
95% CI of LS mean	(77.53, 82.63)	(78.93, 84.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.45 (-2.19, 5.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 16 (MMRM)		
n	235	229
LS mean (SE)	0.33 (0.98)	-0.28 (1.00)
95% CI of LS mean	(-1.60, 2.27)	(-2.24, 1.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.61 (-3.37, 2.14)
Week 24 (MMRM)		
n	239	229
LS mean (SE)	79.22 (1.34)	80.63 (1.36)
95% CI of LS mean	(76.60, 81.85)	(77.96, 83.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.41 (-2.34, 5.16)
Absolute Change at Week 24 (MMRM)		
n	233	227
LS mean (SE)	-0.78 (0.98)	-1.15 (1.00)
95% CI of LS mean	(-2.72, 1.15)	(-3.11, 0.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.36 (-3.12, 2.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52		
n	244	230
Mean (SD)	79.73 (20.86)	83.12 (18.67)
Absolute Change at Week 52		
n	238	227
Mean (SD)	0.21 (16.10)	1.33 (12.28)
Week 52 (MMRM)		
n	237	224
LS mean (SE)	80.00 (1.23)	82.75 (1.26)
95% CI of LS mean	(77.57, 82.42)	(80.27, 85.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.75 (-0.72, 6.22)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	0.12 (0.95)	1.02 (0.97)
95% CI of LS mean	(-1.74, 1.99)	(-0.88, 2.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.90 (-1.77, 3.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	-0.11 (0.76)	-0.14 (0.77)
95% CI of LS mean	(-1.60, 1.38)	(-1.65, 1.38)
P-value within Treatment	0.8860	0.8603
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-2.16, 2.10)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9804
Hedges' G (SE)		0.00 (0.09)
Hedges' 95% CI		(-0.18, 0.18)
Hedges' P-value		0.9804

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	78	71
Mean (SD)	75.45 (22.39)	81.98 (17.93)
Week 8 (MMRM)		
n	79	69
LS mean (SE)	78.34 (2.25)	81.73 (2.41)
95% CI of LS mean	(73.89, 82.79)	(76.96, 86.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.39 (-3.16, 9.93)
Absolute Change at Week 8 (MMRM)		
n	77	68
LS mean (SE)	2.49 (1.58)	-0.48 (1.68)
95% CI of LS mean	(-0.64, 5.61)	(-3.81, 2.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.97 (-7.55, 1.61)
Week 16 (MMRM)		
n	77	67
LS mean (SE)	78.28 (2.44)	80.91 (2.61)
95% CI of LS mean	(73.46, 83.11)	(75.74, 86.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.63 (-4.46, 9.72)

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- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 16 (MMRM)		
n	75	66
LS mean (SE)	2.86 (1.67)	-1.30 (1.77)
95% CI of LS mean	(-0.43, 6.15)	(-4.81, 2.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.16 (-8.99, 0.66)
Week 24 (MMRM)		
n	78	63
LS mean (SE)	75.69 (2.57)	80.50 (2.79)
95% CI of LS mean	(70.61, 80.78)	(74.99, 86.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.81 (-2.70, 12.33)
Absolute Change at Week 24 (MMRM)		
n	76	63
LS mean (SE)	-0.18 (1.58)	-1.32 (1.73)
95% CI of LS mean	(-3.31, 2.96)	(-4.74, 2.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.14 (-5.79, 3.51)

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- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52		
n	78	67
Mean (SD)	78.31 (21.49)	83.62 (18.12)
Absolute Change at Week 52		
n	76	66
Mean (SD)	3.38 (14.02)	1.99 (13.32)
Week 52 (MMRM)		
n	77	64
LS mean (SE)	78.86 (2.18)	82.88 (2.36)
95% CI of LS mean	(74.55, 83.18)	(78.21, 87.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.02 (-2.35, 10.39)
Absolute Change at Week 52 (MMRM)		
n	75	63
LS mean (SE)	3.42 (1.58)	1.02 (1.72)
95% CI of LS mean	(0.30, 6.55)	(-2.37, 4.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.40 (-7.03, 2.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change through Week 52 (MMRM)		
n	77	66
LS mean (SE)	2.04 (1.27)	-0.53 (1.36)
95% CI of LS mean	(-0.47, 4.54)	(-3.23, 2.16)
P-value within Treatment	0.1102	0.6966
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.57 (-6.26, 1.13)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1716
Hedges' G (SE)		-0.23 (0.17)
Hedges' 95% CI		(-0.56, 0.10)
Hedges' P-value		0.1712

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- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	197	207
Mean (SD)	82.67 (19.17)	83.05 (18.91)
Week 8 (MMRM)		
n	197	205
LS mean (SE)	80.99 (1.41)	82.27 (1.38)
95% CI of LS mean	(78.22, 83.76)	(79.55, 84.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.28 (-2.60, 5.16)
Absolute Change at Week 8 (MMRM)		
n	193	203
LS mean (SE)	-1.76 (1.17)	-1.05 (1.14)
95% CI of LS mean	(-4.05, 0.54)	(-3.29, 1.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.70 (-2.51, 3.91)
Week 16 (MMRM)		
n	196	201
LS mean (SE)	82.62 (1.35)	83.12 (1.33)
95% CI of LS mean	(79.97, 85.27)	(80.52, 85.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-3.21, 4.22)

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- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 16 (MMRM)		
n	191	199
LS mean (SE)	0.07 (1.10)	-0.07 (1.07)
95% CI of LS mean	(-2.09, 2.22)	(-2.18, 2.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-3.15, 2.88)
Week 24 (MMRM)		
n	195	202
LS mean (SE)	82.38 (1.36)	82.57 (1.34)
95% CI of LS mean	(79.70, 85.05)	(79.94, 85.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.19 (-3.56, 3.95)
Absolute Change at Week 24 (MMRM)		
n	190	199
LS mean (SE)	-0.32 (1.11)	-0.55 (1.08)
95% CI of LS mean	(-2.50, 1.85)	(-2.67, 1.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-3.27, 2.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52		
n	194	196
Mean (SD)	82.83 (19.73)	84.64 (18.34)
Absolute Change at Week 52		
n	189	193
Mean (SD)	0.18 (17.29)	1.31 (12.16)
Week 52 (MMRM)		
n	192	195
LS mean (SE)	82.79 (1.30)	84.33 (1.28)
95% CI of LS mean	(80.24, 85.35)	(81.80, 86.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.53 (-2.06, 5.13)
Absolute Change at Week 52 (MMRM)		
n	187	192
LS mean (SE)	0.09 (1.09)	1.06 (1.07)
95% CI of LS mean	(-2.05, 2.23)	(-1.04, 3.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.98 (-2.03, 3.98)

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- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change through Week 52 (MMRM)		
n	193	202
LS mean (SE)	-0.06 (0.88)	0.15 (0.86)
95% CI of LS mean	(-1.79, 1.68)	(-1.55, 1.84)
P-value within Treatment	0.9480	0.8637
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.21 (-2.22, 2.63)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8677
Hedges' G (SE)		0.02 (0.10)
Hedges' 95% CI		(-0.18, 0.21)
Hedges' P-value		0.8676

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- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	140	146
Mean (SD)	84.00 (18.26)	86.96 (17.04)
Week 8 (MMRM)		
n	134	143
LS mean (SE)	82.99 (1.63)	86.16 (1.57)
95% CI of LS mean	(79.79, 86.19)	(83.06, 89.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.17 (-1.31, 7.64)
Absolute Change at Week 8 (MMRM)		
n	130	141
LS mean (SE)	-1.28 (1.39)	-1.03 (1.34)
95% CI of LS mean	(-4.02, 1.46)	(-3.66, 1.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.25 (-3.56, 4.06)
Week 16 (MMRM)		
n	130	139
LS mean (SE)	85.83 (1.40)	87.38 (1.36)
95% CI of LS mean	(83.06, 88.59)	(84.70, 90.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.55 (-2.32, 5.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 16 (MMRM)		
n	126	137
LS mean (SE)	2.00 (1.18)	0.47 (1.14)
95% CI of LS mean	(-0.33, 4.32)	(-1.76, 2.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.52 (-4.76, 1.72)
Week 24 (MMRM)		
n	132	140
LS mean (SE)	84.63 (1.43)	87.60 (1.39)
95% CI of LS mean	(81.80, 87.45)	(84.85, 90.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.97 (-0.99, 6.93)
Absolute Change at Week 24 (MMRM)		
n	128	137
LS mean (SE)	0.49 (1.15)	0.79 (1.12)
95% CI of LS mean	(-1.78, 2.76)	(-1.41, 2.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.30 (-2.88, 3.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52		
n	139	143
Mean (SD)	84.38 (18.68)	87.62 (17.49)
Absolute Change at Week 52		
n	135	140
Mean (SD)	0.84 (14.92)	0.89 (11.18)
Week 52 (MMRM)		
n	132	139
LS mean (SE)	84.56 (1.50)	87.78 (1.46)
95% CI of LS mean	(81.61, 87.50)	(84.91, 90.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.22 (-0.91, 7.36)
Absolute Change at Week 52 (MMRM)		
n	128	136
LS mean (SE)	0.67 (1.16)	0.84 (1.12)
95% CI of LS mean	(-1.61, 2.95)	(-1.37, 3.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-3.02, 3.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change through Week 52 (MMRM)		
n	130	139
LS mean (SE)	1.05 (0.95)	0.70 (0.92)
95% CI of LS mean	(-0.82, 2.92)	(-1.11, 2.51)
P-value within Treatment	0.2693	0.4458
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.35 (-2.96, 2.26)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7924
Hedges' G (SE)		-0.03 (0.12)
Hedges' 95% CI		(-0.27, 0.21)
Hedges' P-value		0.7912

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	142	134
Mean (SD)	77.37 (21.70)	78.33 (19.24)
Week 8 (MMRM)		
n	142	131
LS mean (SE)	77.83 (1.74)	77.47 (1.81)
95% CI of LS mean	(74.40, 81.26)	(73.90, 81.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.36 (-5.34, 4.62)
Absolute Change at Week 8 (MMRM)		
n	140	130
LS mean (SE)	-0.27 (1.31)	-0.34 (1.36)
95% CI of LS mean	(-2.85, 2.31)	(-3.01, 2.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-3.81, 3.67)
Week 16 (MMRM)		
n	143	129
LS mean (SE)	77.48 (1.84)	76.96 (1.92)
95% CI of LS mean	(73.86, 81.11)	(73.17, 80.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.52 (-5.79, 4.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 16 (MMRM)		
n	140	128
LS mean (SE)	-0.55 (1.41)	-0.91 (1.46)
95% CI of LS mean	(-3.32, 2.21)	(-3.79, 1.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.35 (-4.36, 3.66)
Week 24 (MMRM)		
n	141	125
LS mean (SE)	76.77 (1.88)	75.70 (1.98)
95% CI of LS mean	(73.07, 80.48)	(71.81, 79.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.07 (-6.47, 4.33)
Absolute Change at Week 24 (MMRM)		
n	138	125
LS mean (SE)	-1.42 (1.41)	-1.99 (1.48)
95% CI of LS mean	(-4.21, 1.36)	(-4.90, 0.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.57 (-4.62, 3.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52		
n	138	122
Mean (SD)	78.45 (21.62)	80.57 (18.45)
Absolute Change at Week 52		
n	135	121
Mean (SD)	1.21 (17.88)	2.04 (13.76)
Week 52 (MMRM)		
n	137	120
LS mean (SE)	79.17 (1.65)	79.44 (1.73)
95% CI of LS mean	(75.93, 82.42)	(76.03, 82.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.27 (-4.47, 5.01)
Absolute Change at Week 52 (MMRM)		
n	134	119
LS mean (SE)	0.99 (1.39)	1.65 (1.46)
95% CI of LS mean	(-1.74, 3.73)	(-1.22, 4.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.65 (-3.33, 4.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change through Week 52 (MMRM)		
n	140	129
LS mean (SE)	-0.33 (1.11)	-0.42 (1.16)
95% CI of LS mean	(-2.52, 1.87)	(-2.70, 1.87)
P-value within Treatment	0.7692	0.7201
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-3.28, 3.10)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9562
Hedges' G (SE)		-0.01 (0.12)
Hedges' 95% CI		(-0.25, 0.23)
Hedges' P-value		0.9559

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	102	111
Mean (SD)	81.06 (20.58)	84.45 (18.41)
Week 8 (MMRM)		
n	98	112
LS mean (SE)	77.95 (2.06)	83.69 (1.93)
95% CI of LS mean	(73.89, 82.02)	(79.89, 87.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.74 (0.17, 11.32)
Absolute Change at Week 8 (MMRM)		
n	97	109
LS mean (SE)	-2.94 (1.57)	-1.50 (1.48)
95% CI of LS mean	(-6.03, 0.15)	(-4.41, 1.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.45 (-2.80, 5.70)
Week 16 (MMRM)		
n	96	108
LS mean (SE)	79.80 (1.88)	84.66 (1.77)
95% CI of LS mean	(76.09, 83.51)	(81.17, 88.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.86 (-0.24, 9.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 16 (MMRM)		
n	95	105
LS mean (SE)	-1.06 (1.29)	-0.26 (1.22)
95% CI of LS mean	(-3.59, 1.48)	(-2.67, 2.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.80 (-2.70, 4.30)
Week 24 (MMRM)		
n	97	108
LS mean (SE)	79.31 (2.01)	83.87 (1.89)
95% CI of LS mean	(75.36, 83.27)	(80.13, 87.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.55 (-0.89, 10.00)
Absolute Change at Week 24 (MMRM)		
n	96	106
LS mean (SE)	-1.59 (1.24)	-1.00 (1.18)
95% CI of LS mean	(-4.02, 0.85)	(-3.31, 1.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.59 (-2.78, 3.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52		
n	101	104
Mean (SD)	80.75 (21.50)	85.99 (16.99)
Absolute Change at Week 52		
n	100	101
Mean (SD)	-0.12 (11.82)	1.47 (9.74)
Week 52 (MMRM)		
n	97	104
LS mean (SE)	80.55 (1.86)	85.99 (1.76)
95% CI of LS mean	(76.89, 84.22)	(82.52, 89.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.43 (0.38, 10.49)
Absolute Change at Week 52 (MMRM)		
n	96	101
LS mean (SE)	-0.30 (1.10)	1.28 (1.07)
95% CI of LS mean	(-2.47, 1.87)	(-0.82, 3.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.58 (-1.44, 4.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change through Week 52 (MMRM)		
n	98	107
LS mean (SE)	-0.98 (0.93)	0.01 (0.89)
95% CI of LS mean	(-2.82, 0.86)	(-1.75, 1.76)
P-value within Treatment	0.2931	0.9925
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.99 (-1.56, 3.54)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4441
Hedges' G (SE)		0.11 (0.14)
Hedges' 95% CI		(-0.17, 0.38)
Hedges' P-value		0.4434

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	180	169
Mean (SD)	80.44 (20.20)	81.76 (18.70)
Week 8 (MMRM)		
n	178	162
LS mean (SE)	81.41 (1.47)	81.19 (1.54)
95% CI of LS mean	(78.53, 84.29)	(78.17, 84.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-4.40, 3.96)
Absolute Change at Week 8 (MMRM)		
n	173	162
LS mean (SE)	0.80 (1.20)	-0.49 (1.24)
95% CI of LS mean	(-1.56, 3.16)	(-2.93, 1.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.30 (-4.69, 2.10)
Week 16 (MMRM)		
n	177	160
LS mean (SE)	82.17 (1.52)	81.21 (1.60)
95% CI of LS mean	(79.18, 85.16)	(78.07, 84.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.96 (-5.30, 3.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	171	160
LS mean (SE)	1.91 (1.24)	-0.45 (1.28)
95% CI of LS mean	(-0.53, 4.35)	(-2.97, 2.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.36 (-5.87, 1.16)
Week 24 (MMRM)		
n	176	157
LS mean (SE)	80.99 (1.52)	80.94 (1.60)
95% CI of LS mean	(78.00, 83.98)	(77.79, 84.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-4.40, 4.29)
Absolute Change at Week 24 (MMRM)		
n	170	156
LS mean (SE)	0.38 (1.25)	-0.57 (1.30)
95% CI of LS mean	(-2.07, 2.83)	(-3.12, 1.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.95 (-4.49, 2.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52		
n	176	161
Mean (SD)	81.82 (19.77)	83.32 (18.99)
Absolute Change at Week 52		
n	170	160
Mean (SD)	1.70 (18.62)	1.40 (13.89)
Week 52 (MMRM)		
n	172	155
LS mean (SE)	82.18 (1.41)	82.61 (1.48)
95% CI of LS mean	(79.40, 84.96)	(79.69, 85.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-3.60, 4.47)
Absolute Change at Week 52 (MMRM)		
n	166	154
LS mean (SE)	1.73 (1.28)	0.87 (1.33)
95% CI of LS mean	(-0.80, 4.25)	(-1.75, 3.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.86 (-4.50, 2.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	172	161
LS mean (SE)	1.34 (1.02)	-0.05 (1.05)
95% CI of LS mean	(-0.66, 3.34)	(-2.12, 2.02)
P-value within Treatment	0.1881	0.9633
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.39 (-4.27, 1.49)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3440
Hedges' G (SE)		-0.10 (0.11)
Hedges' 95% CI		(-0.32, 0.11)
Hedges' P-value		0.3435

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	163	152
Mean (SD)	85.07 (16.65)	86.68 (17.27)
Week 8 (MMRM)		
n	161	151
LS mean (SE)	84.20 (1.34)	86.52 (1.38)
95% CI of LS mean	(81.56, 86.84)	(83.80, 89.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.32 (-1.47, 6.12)
Absolute Change at Week 8 (MMRM)		
n	158	149
LS mean (SE)	-1.02 (1.11)	-0.27 (1.14)
95% CI of LS mean	(-3.21, 1.16)	(-2.52, 1.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.75 (-2.38, 3.89)
Week 16 (MMRM)		
n	156	149
LS mean (SE)	84.88 (1.38)	85.91 (1.41)
95% CI of LS mean	(82.17, 87.59)	(83.14, 88.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.04 (-2.85, 4.92)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 16 (MMRM)		
n	153	147
LS mean (SE)	-0.14 (1.16)	-0.67 (1.19)
95% CI of LS mean	(-2.43, 2.14)	(-3.00, 1.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.52 (-3.79, 2.75)
Week 24 (MMRM)		
n	156	147
LS mean (SE)	84.04 (1.49)	84.45 (1.53)
95% CI of LS mean	(81.11, 86.98)	(81.43, 87.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.41 (-3.80, 4.62)
Absolute Change at Week 24 (MMRM)		
n	153	145
LS mean (SE)	-0.98 (1.32)	-2.13 (1.35)
95% CI of LS mean	(-3.56, 1.61)	(-4.79, 0.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.15 (-4.87, 2.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52		
n	159	144
Mean (SD)	84.91 (18.54)	88.31 (15.05)
Absolute Change at Week 52		
n	156	142
Mean (SD)	0.27 (16.10)	1.00 (14.16)
Week 52 (MMRM)		
n	155	143
LS mean (SE)	85.09 (1.36)	87.95 (1.41)
95% CI of LS mean	(82.40, 87.77)	(85.17, 90.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.87 (-1.00, 6.73)
Absolute Change at Week 52 (MMRM)		
n	152	141
LS mean (SE)	0.03 (1.25)	1.17 (1.29)
95% CI of LS mean	(-2.43, 2.50)	(-1.38, 3.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.14 (-2.41, 4.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	-0.36 (0.99)	-0.54 (1.02)
95% CI of LS mean	(-2.31, 1.59)	(-2.54, 1.46)
P-value within Treatment	0.7148	0.5949
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-2.97, 2.62)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8999
Hedges' G (SE)		-0.01 (0.11)
Hedges' 95% CI		(-0.24, 0.21)
Hedges' P-value		0.8998

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	103	109
Mean (SD)	88.92 (13.78)	86.77 (15.39)
Week 8 (MMRM)		
n	106	108
LS mean (SE)	89.82 (1.40)	88.62 (1.38)
95% CI of LS mean	(87.07, 92.57)	(85.90, 91.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.20 (-5.08, 2.68)
Absolute Change at Week 8 (MMRM)		
n	103	107
LS mean (SE)	1.04 (1.23)	1.83 (1.20)
95% CI of LS mean	(-1.38, 3.46)	(-0.54, 4.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.79 (-2.61, 4.18)
Week 16 (MMRM)		
n	105	106
LS mean (SE)	89.23 (1.45)	87.82 (1.44)
95% CI of LS mean	(86.38, 92.09)	(84.99, 90.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.41 (-5.45, 2.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 16 (MMRM)		
n	102	105
LS mean (SE)	0.30 (1.27)	1.03 (1.24)
95% CI of LS mean	(-2.20, 2.80)	(-1.43, 3.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.73 (-2.78, 4.24)
Week 24 (MMRM)		
n	106	103
LS mean (SE)	88.95 (1.42)	88.96 (1.42)
95% CI of LS mean	(86.16, 91.75)	(86.16, 91.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-3.96, 3.98)
Absolute Change at Week 24 (MMRM)		
n	103	103
LS mean (SE)	0.07 (1.36)	2.09 (1.35)
95% CI of LS mean	(-2.62, 2.75)	(-0.57, 4.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.03 (-1.77, 5.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52		
n	104	102
Mean (SD)	90.20 (14.24)	90.03 (12.41)
Absolute Change at Week 52		
n	101	101
Mean (SD)	1.05 (13.63)	2.89 (11.21)
Week 52 (MMRM)		
n	104	101
LS mean (SE)	90.24 (1.33)	89.78 (1.34)
95% CI of LS mean	(87.61, 92.87)	(87.14, 92.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.46 (-4.20, 3.28)
Absolute Change at Week 52 (MMRM)		
n	101	100
LS mean (SE)	1.07 (1.24)	2.97 (1.24)
95% CI of LS mean	(-1.38, 3.52)	(0.54, 5.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.90 (-1.56, 5.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change through Week 52 (MMRM)		
n	103	106
LS mean (SE)	0.48 (1.07)	2.03 (1.06)
95% CI of LS mean	(-1.63, 2.59)	(-0.05, 4.11)
P-value within Treatment	0.6550	0.0557
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.55 (-1.42, 4.53)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3050
Hedges' G (SE)		0.14 (0.14)
Hedges' 95% CI		(-0.13, 0.41)
Hedges' P-value		0.3037

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	24	26
Mean (SD)	91.32 (10.56)	83.97 (18.09)
Week 8 (MMRM)		
n	24	23
LS mean (SE)	93.21 (3.14)	89.78 (3.11)
95% CI of LS mean	(86.85, 99.57)	(83.51, 96.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.43 (-12.44, 5.59)
Absolute Change at Week 8 (MMRM)		
n	24	23
LS mean (SE)	2.64 (2.51)	3.84 (2.49)
95% CI of LS mean	(-2.52, 7.79)	(-1.26, 8.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.20 (-6.16, 8.57)
Week 16 (MMRM)		
n	22	23
LS mean (SE)	93.44 (3.12)	87.14 (3.05)
95% CI of LS mean	(87.11, 99.77)	(80.95, 93.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.30 (-15.22, 2.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 16 (MMRM)		
n	22	23
LS mean (SE)	2.58 (3.08)	2.12 (3.01)
95% CI of LS mean	(-3.67, 8.83)	(-3.98, 8.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-9.28, 8.35)
Week 24 (MMRM)		
n	22	22
LS mean (SE)	90.76 (2.34)	90.03 (2.32)
95% CI of LS mean	(85.98, 95.55)	(85.30, 94.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.73 (-7.56, 6.10)
Absolute Change at Week 24 (MMRM)		
n	22	22
LS mean (SE)	-0.70 (3.16)	3.34 (3.10)
95% CI of LS mean	(-7.08, 5.67)	(-2.92, 9.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.04 (-4.98, 13.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52		
n	22	20
Mean (SD)	93.56 (7.24)	91.25 (9.92)
Absolute Change at Week 52		
n	22	20
Mean (SD)	1.52 (9.84)	1.67 (10.33)
Week 52 (MMRM)		
n	22	20
LS mean (SE)	93.31 (2.06)	90.02 (2.15)
95% CI of LS mean	(89.10, 97.53)	(85.64, 94.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.30 (-9.49, 2.89)
Absolute Change at Week 52 (MMRM)		
n	22	20
LS mean (SE)	2.17 (2.23)	2.40 (2.31)
95% CI of LS mean	(-2.44, 6.77)	(-2.34, 7.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.24 (-6.49, 6.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change through Week 52 (MMRM)		
n	22	24
LS mean (SE)	1.35 (2.46)	2.62 (2.41)
95% CI of LS mean	(-3.62, 6.32)	(-2.26, 7.49)
P-value within Treatment	0.5862	0.2840
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.27 (-5.81, 8.34)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7187
Hedges' G (SE)		0.11 (0.29)
Hedges' 95% CI		(-0.48, 0.69)
Hedges' P-value		0.7146

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	86.19 (15.98)	87.05 (16.22)
Week 8 (MMRM)		
n	243	236
LS mean (SE)	85.73 (1.03)	87.22 (1.05)
95% CI of LS mean	(83.70, 87.75)	(85.16, 89.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.49 (-1.40, 4.38)
Absolute Change at Week 8 (MMRM)		
n	237	233
LS mean (SE)	-0.41 (0.88)	0.22 (0.89)
95% CI of LS mean	(-2.15, 1.32)	(-1.53, 1.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-1.83, 3.09)
Week 16 (MMRM)		
n	239	232
LS mean (SE)	85.88 (1.07)	86.69 (1.08)
95% CI of LS mean	(83.78, 87.97)	(84.56, 88.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.81 (-2.17, 3.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 16 (MMRM)		
n	233	229
LS mean (SE)	-0.21 (0.90)	-0.26 (0.91)
95% CI of LS mean	(-1.98, 1.56)	(-2.04, 1.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-2.56, 2.47)
Week 24 (MMRM)		
n	240	228
LS mean (SE)	85.55 (1.13)	86.06 (1.15)
95% CI of LS mean	(83.33, 87.76)	(83.80, 88.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.52 (-2.65, 3.69)
Absolute Change at Week 24 (MMRM)		
n	234	226
LS mean (SE)	-0.50 (1.00)	-0.83 (1.02)
95% CI of LS mean	(-2.48, 1.47)	(-2.84, 1.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-3.14, 2.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52		
n	244	230
Mean (SD)	86.57 (17.61)	88.77 (14.34)
Absolute Change at Week 52		
n	238	227
Mean (SD)	0.55 (15.49)	1.65 (13.56)
Week 52 (MMRM)		
n	237	224
LS mean (SE)	86.53 (1.04)	88.65 (1.07)
95% CI of LS mean	(84.48, 88.58)	(86.55, 90.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.12 (-0.82, 5.06)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	0.33 (0.95)	1.78 (0.97)
95% CI of LS mean	(-1.54, 2.21)	(-0.13, 3.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.45 (-1.23, 4.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	-0.13 (0.76)	0.23 (0.77)
95% CI of LS mean	(-1.63, 1.38)	(-1.29, 1.75)
P-value within Treatment	0.8680	0.7664
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-1.78, 2.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7432
Hedges' G (SE)		0.03 (0.09)
Hedges' 95% CI		(-0.15, 0.21)
Hedges' P-value		0.7429

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	77	70
Mean (SD)	86.04 (15.08)	86.90 (17.70)
Week 8 (MMRM)		
n	78	67
LS mean (SE)	86.15 (1.92)	87.91 (2.06)
95% CI of LS mean	(82.36, 89.94)	(83.84, 91.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.75 (-3.82, 7.33)
Absolute Change at Week 8 (MMRM)		
n	76	66
LS mean (SE)	-0.05 (1.72)	1.30 (1.84)
95% CI of LS mean	(-3.45, 3.36)	(-2.34, 4.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.35 (-3.65, 6.35)
Week 16 (MMRM)		
n	76	66
LS mean (SE)	84.91 (2.06)	87.18 (2.21)
95% CI of LS mean	(80.84, 88.99)	(82.81, 91.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.27 (-3.72, 8.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 16 (MMRM)		
n	74	65
LS mean (SE)	-0.87 (1.80)	0.84 (1.92)
95% CI of LS mean	(-4.44, 2.69)	(-2.97, 4.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.71 (-3.52, 6.93)
Week 24 (MMRM)		
n	78	62
LS mean (SE)	82.41 (2.16)	86.67 (2.39)
95% CI of LS mean	(78.14, 86.69)	(81.94, 91.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.26 (-2.13, 10.65)
Absolute Change at Week 24 (MMRM)		
n	76	62
LS mean (SE)	-3.67 (2.08)	0.36 (2.28)
95% CI of LS mean	(-7.78, 0.44)	(-4.15, 4.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.03 (-2.08, 10.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52		
n	77	65
Mean (SD)	87.88 (15.62)	87.95 (16.27)
Absolute Change at Week 52		
n	75	64
Mean (SD)	1.78 (10.99)	0.13 (14.51)
Week 52 (MMRM)		
n	76	62
LS mean (SE)	88.01 (1.83)	88.09 (2.00)
95% CI of LS mean	(84.38, 91.64)	(84.13, 92.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-5.30, 5.47)
Absolute Change at Week 52 (MMRM)		
n	74	61
LS mean (SE)	1.76 (1.45)	1.48 (1.59)
95% CI of LS mean	(-1.11, 4.63)	(-1.66, 4.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.28 (-4.54, 3.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change through Week 52 (MMRM)		
n	76	65
LS mean (SE)	-0.93 (1.40)	0.89 (1.52)
95% CI of LS mean	(-3.70, 1.85)	(-2.11, 3.89)
P-value within Treatment	0.5099	0.5570
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.82 (-2.28, 5.92)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3816
Hedges' G (SE)		0.15 (0.17)
Hedges' 95% CI		(-0.18, 0.48)
Hedges' P-value		0.3805

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	187	194
Mean (SD)	87.03 (15.82)	86.60 (16.01)
Week 8 (MMRM)		
n	189	192
LS mean (SE)	86.53 (1.14)	87.23 (1.13)
95% CI of LS mean	(84.29, 88.77)	(85.01, 89.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.69 (-2.46, 3.85)
Absolute Change at Week 8 (MMRM)		
n	185	190
LS mean (SE)	-0.26 (0.94)	0.38 (0.93)
95% CI of LS mean	(-2.11, 1.60)	(-1.45, 2.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-1.98, 3.24)
Week 16 (MMRM)		
n	185	189
LS mean (SE)	87.28 (1.15)	86.55 (1.13)
95% CI of LS mean	(85.03, 89.54)	(84.32, 88.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.73 (-3.90, 2.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 16 (MMRM)		
n	181	187
LS mean (SE)	0.37 (0.97)	-0.25 (0.96)
95% CI of LS mean	(-1.54, 2.29)	(-2.13, 1.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.62 (-3.31, 2.07)
Week 24 (MMRM)		
n	184	188
LS mean (SE)	87.49 (1.19)	86.21 (1.18)
95% CI of LS mean	(85.15, 89.83)	(83.89, 88.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.29 (-4.58, 2.00)
Absolute Change at Week 24 (MMRM)		
n	180	186
LS mean (SE)	0.74 (1.03)	-0.61 (1.02)
95% CI of LS mean	(-1.29, 2.77)	(-2.61, 1.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.36 (-4.20, 1.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52		
n	185	183
Mean (SD)	86.88 (17.62)	89.25 (13.24)
Absolute Change at Week 52		
n	181	181
Mean (SD)	0.08 (16.62)	2.21 (12.93)
Week 52 (MMRM)		
n	183	182
LS mean (SE)	86.73 (1.16)	88.92 (1.15)
95% CI of LS mean	(84.46, 89.01)	(86.66, 91.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.19 (-1.03, 5.40)
Absolute Change at Week 52 (MMRM)		
n	179	180
LS mean (SE)	-0.15 (1.10)	2.03 (1.09)
95% CI of LS mean	(-2.31, 2.02)	(-0.12, 4.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.18 (-0.87, 5.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change through Week 52 (MMRM)		
n	183	189
LS mean (SE)	0.32 (0.85)	0.39 (0.83)
95% CI of LS mean	(-1.34, 1.99)	(-1.25, 2.03)
P-value within Treatment	0.7030	0.6399
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-2.27, 2.40)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9548
Hedges' G (SE)		0.01 (0.10)
Hedges' 95% CI		(-0.20, 0.21)
Hedges' P-value		0.9547

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	133	141
Mean (SD)	88.16 (14.40)	89.07 (14.98)
Week 8 (MMRM)		
n	130	139
LS mean (SE)	86.69 (1.43)	89.09 (1.38)
95% CI of LS mean	(83.88, 89.50)	(86.37, 91.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.40 (-1.53, 6.32)
Absolute Change at Week 8 (MMRM)		
n	127	137
LS mean (SE)	-1.45 (1.19)	-0.03 (1.14)
95% CI of LS mean	(-3.79, 0.89)	(-2.29, 2.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.42 (-1.84, 4.68)
Week 16 (MMRM)		
n	125	135
LS mean (SE)	87.93 (1.31)	89.09 (1.26)
95% CI of LS mean	(85.35, 90.50)	(86.60, 91.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.16 (-2.45, 4.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 16 (MMRM)		
n	122	133
LS mean (SE)	-0.04 (1.03)	0.08 (0.99)
95% CI of LS mean	(-2.08, 2.00)	(-1.87, 2.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-2.72, 2.96)
Week 24 (MMRM)		
n	127	134
LS mean (SE)	87.18 (1.45)	88.12 (1.41)
95% CI of LS mean	(84.33, 90.04)	(85.35, 90.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (-3.07, 4.93)
Absolute Change at Week 24 (MMRM)		
n	124	132
LS mean (SE)	-0.82 (1.21)	-0.90 (1.17)
95% CI of LS mean	(-3.20, 1.56)	(-3.21, 1.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-3.41, 3.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52		
n	132	137
Mean (SD)	87.67 (17.61)	90.45 (15.04)
Absolute Change at Week 52		
n	129	135
Mean (SD)	-0.34 (14.11)	1.54 (13.63)
Week 52 (MMRM)		
n	126	133
LS mean (SE)	87.27 (1.45)	90.47 (1.40)
95% CI of LS mean	(84.43, 90.12)	(87.71, 93.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.20 (-0.79, 7.19)
Absolute Change at Week 52 (MMRM)		
n	123	131
LS mean (SE)	-0.90 (1.25)	1.53 (1.21)
95% CI of LS mean	(-3.36, 1.55)	(-0.84, 3.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.43 (-0.99, 5.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change through Week 52 (MMRM)		
n	125	134
LS mean (SE)	-0.59 (0.94)	0.24 (0.90)
95% CI of LS mean	(-2.43, 1.26)	(-1.54, 2.02)
P-value within Treatment	0.5314	0.7933
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.82 (-1.75, 3.40)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5298
Hedges' G (SE)		0.08 (0.12)
Hedges' 95% CI		(-0.17, 0.32)
Hedges' P-value		0.5275

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	136	125
Mean (SD)	85.17 (16.66)	84.13 (17.56)
Week 8 (MMRM)		
n	137	120
LS mean (SE)	86.30 (1.36)	85.35 (1.45)
95% CI of LS mean	(83.61, 88.99)	(82.50, 88.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.95 (-4.89, 2.99)
Absolute Change at Week 8 (MMRM)		
n	134	119
LS mean (SE)	0.99 (1.16)	1.34 (1.23)
95% CI of LS mean	(-1.30, 3.28)	(-1.07, 3.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.35 (-2.99, 3.70)
Week 16 (MMRM)		
n	136	120
LS mean (SE)	85.54 (1.53)	83.87 (1.62)
95% CI of LS mean	(82.53, 88.55)	(80.68, 87.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.67 (-6.07, 2.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 16 (MMRM)		
n	133	119
LS mean (SE)	0.10 (1.39)	-0.01 (1.46)
95% CI of LS mean	(-2.64, 2.83)	(-2.89, 2.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-4.10, 3.88)
Week 24 (MMRM)		
n	135	116
LS mean (SE)	84.99 (1.55)	84.14 (1.65)
95% CI of LS mean	(81.94, 88.03)	(80.89, 87.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.84 (-5.32, 3.63)
Absolute Change at Week 24 (MMRM)		
n	132	116
LS mean (SE)	-0.32 (1.50)	0.23 (1.59)
95% CI of LS mean	(-3.27, 2.63)	(-2.90, 3.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.55 (-3.76, 4.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52		
n	134	113
Mean (SD)	86.63 (16.64)	87.17 (12.55)
Absolute Change at Week 52		
n	131	112
Mean (SD)	1.59 (15.98)	1.79 (12.97)
Week 52 (MMRM)		
n	133	111
LS mean (SE)	87.08 (1.32)	86.66 (1.42)
95% CI of LS mean	(84.48, 89.67)	(83.86, 89.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.41 (-4.25, 3.43)
Absolute Change at Week 52 (MMRM)		
n	130	110
LS mean (SE)	1.68 (1.29)	2.42 (1.38)
95% CI of LS mean	(-0.86, 4.22)	(-0.30, 5.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.75 (-3.00, 4.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change through Week 52 (MMRM)		
n	134	120
LS mean (SE)	0.48 (1.13)	0.88 (1.20)
95% CI of LS mean	(-1.75, 2.72)	(-1.48, 3.24)
P-value within Treatment	0.6704	0.4633
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.40 (-2.87, 3.67)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8111
Hedges' G (SE)		0.03 (0.13)
Hedges' 95% CI		(-0.22, 0.28)
Hedges' P-value		0.8101

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	99	108
Mean (SD)	87.63 (16.68)	90.43 (12.42)
Week 8 (MMRM)		
n	96	109
LS mean (SE)	85.68 (1.50)	89.97 (1.40)
95% CI of LS mean	(82.73, 88.63)	(87.21, 92.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.29 (0.25, 8.34)
Absolute Change at Week 8 (MMRM)		
n	95	106
LS mean (SE)	-1.54 (1.18)	-0.80 (1.12)
95% CI of LS mean	(-3.87, 0.80)	(-3.01, 1.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.74 (-2.48, 3.95)
Week 16 (MMRM)		
n	94	105
LS mean (SE)	86.77 (1.46)	90.36 (1.38)
95% CI of LS mean	(83.88, 89.65)	(87.65, 93.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.60 (-0.37, 7.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 16 (MMRM)		
n	93	102
LS mean (SE)	-0.52 (1.05)	-0.31 (1.00)
95% CI of LS mean	(-2.59, 1.55)	(-2.28, 1.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.21 (-2.65, 3.07)
Week 24 (MMRM)		
n	95	104
LS mean (SE)	87.53 (1.51)	89.31 (1.43)
95% CI of LS mean	(84.55, 90.51)	(86.50, 92.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.79 (-2.32, 5.89)
Absolute Change at Week 24 (MMRM)		
n	94	102
LS mean (SE)	0.34 (1.20)	-1.31 (1.14)
95% CI of LS mean	(-2.02, 2.70)	(-3.56, 0.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.65 (-4.91, 1.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52		
n	98	101
Mean (SD)	87.22 (17.30)	90.43 (13.56)
Absolute Change at Week 52		
n	97	98
Mean (SD)	-0.03 (14.08)	0.09 (11.57)
Week 52 (MMRM)		
n	94	101
LS mean (SE)	86.94 (1.58)	90.69 (1.50)
95% CI of LS mean	(83.84, 90.05)	(87.74, 93.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.75 (-0.55, 8.04)
Absolute Change at Week 52 (MMRM)		
n	93	98
LS mean (SE)	-0.23 (1.36)	0.22 (1.31)
95% CI of LS mean	(-2.90, 2.45)	(-2.37, 2.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-3.28, 4.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change through Week 52 (MMRM)		
n	95	104
LS mean (SE)	-0.14 (0.99)	-0.47 (0.94)
95% CI of LS mean	(-2.09, 1.81)	(-2.33, 1.40)
P-value within Treatment	0.8907	0.6214
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-3.03, 2.37)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8093
Hedges' G (SE)		-0.03 (0.14)
Hedges' 95% CI		(-0.31, 0.24)
Hedges' P-value		0.8090

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	170	158
Mean (SD)	86.08 (15.00)	84.23 (18.25)
Week 8 (MMRM)		
n	171	150
LS mean (SE)	86.80 (1.29)	85.59 (1.37)
95% CI of LS mean	(84.26, 89.33)	(82.89, 88.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.21 (-4.91, 2.50)
Absolute Change at Week 8 (MMRM)		
n	166	150
LS mean (SE)	0.55 (1.12)	1.58 (1.18)
95% CI of LS mean	(-1.66, 2.76)	(-0.73, 3.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.03 (-2.18, 4.24)
Week 16 (MMRM)		
n	167	150
LS mean (SE)	86.46 (1.35)	84.15 (1.43)
95% CI of LS mean	(83.80, 89.11)	(81.34, 86.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.31 (-6.18, 1.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	162	150
LS mean (SE)	0.32 (1.23)	0.28 (1.28)
95% CI of LS mean	(-2.09, 2.74)	(-2.24, 2.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-3.54, 3.45)
Week 24 (MMRM)		
n	167	146
LS mean (SE)	85.05 (1.42)	84.25 (1.52)
95% CI of LS mean	(82.25, 87.86)	(81.26, 87.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.80 (-4.91, 3.30)
Absolute Change at Week 24 (MMRM)		
n	162	146
LS mean (SE)	-1.11 (1.36)	0.32 (1.43)
95% CI of LS mean	(-3.79, 1.56)	(-2.49, 3.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.43 (-2.45, 5.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52		
n	168	149
Mean (SD)	87.10 (17.03)	87.98 (14.32)
Absolute Change at Week 52		
n	163	149
Mean (SD)	1.02 (15.68)	2.68 (14.28)
Week 52 (MMRM)		
n	165	143
LS mean (SE)	87.17 (1.24)	87.39 (1.32)
95% CI of LS mean	(84.73, 89.60)	(84.79, 90.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.23 (-3.34, 3.80)
Absolute Change at Week 52 (MMRM)		
n	160	143
LS mean (SE)	0.80 (1.18)	3.11 (1.25)
95% CI of LS mean	(-1.53, 3.12)	(0.66, 5.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.32 (-1.07, 5.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	150
LS mean (SE)	0.00 (1.01)	1.24 (1.06)
95% CI of LS mean	(-1.99, 1.99)	(-0.85, 3.33)
P-value within Treatment	0.9975	0.2433
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.24 (-1.65, 4.13)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4003
Hedges' G (SE)		0.10 (0.11)
Hedges' 95% CI		(-0.13, 0.32)
Hedges' P-value		0.3996

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	164	152
Mean (SD)	71.48 (18.66)	75.22 (17.41)
Week 8 (MMRM)		
n	161	153
LS mean (SE)	72.18 (1.39)	75.39 (1.43)
95% CI of LS mean	(69.44, 74.93)	(72.57, 78.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.21 (-0.73, 7.14)
Absolute Change at Week 8 (MMRM)		
n	158	151
LS mean (SE)	0.64 (1.13)	0.14 (1.16)
95% CI of LS mean	(-1.59, 2.86)	(-2.14, 2.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.49 (-3.68, 2.70)
Week 16 (MMRM)		
n	158	148
LS mean (SE)	74.25 (1.40)	75.19 (1.44)
95% CI of LS mean	(71.49, 77.00)	(72.35, 78.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.95 (-3.01, 4.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 16 (MMRM)		
n	155	146
LS mean (SE)	2.77 (1.13)	0.08 (1.16)
95% CI of LS mean	(0.55, 5.00)	(-2.21, 2.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.69 (-5.89, 0.50)
Week 24 (MMRM)		
n	156	147
LS mean (SE)	72.26 (1.43)	76.67 (1.48)
95% CI of LS mean	(69.44, 75.09)	(73.76, 79.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.40 (0.35, 8.46)
Absolute Change at Week 24 (MMRM)		
n	153	145
LS mean (SE)	0.78 (1.15)	1.56 (1.18)
95% CI of LS mean	(-1.49, 3.05)	(-0.77, 3.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.78 (-2.47, 4.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52		
n	159	145
Mean (SD)	74.33 (19.53)	78.43 (18.19)
Absolute Change at Week 52		
n	156	143
Mean (SD)	3.28 (14.24)	3.11 (13.55)
Week 52 (MMRM)		
n	155	144
LS mean (SE)	74.30 (1.48)	78.03 (1.53)
95% CI of LS mean	(71.38, 77.22)	(75.02, 81.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.73 (-0.47, 7.92)
Absolute Change at Week 52 (MMRM)		
n	152	142
LS mean (SE)	2.94 (1.13)	2.95 (1.16)
95% CI of LS mean	(0.71, 5.16)	(0.66, 5.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-3.18, 3.21)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	2.16 (0.95)	1.53 (0.98)
95% CI of LS mean	(0.29, 4.04)	(-0.39, 3.45)
P-value within Treatment	0.0238	0.1187
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.63 (-3.32, 2.05)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6429
Hedges' G (SE)		-0.05 (0.11)
Hedges' 95% CI		(-0.28, 0.17)
Hedges' P-value		0.6426

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	115	123
Mean (SD)	74.22 (16.61)	75.19 (18.57)
Week 8 (MMRM)		
n	116	120
LS mean (SE)	76.06 (1.60)	76.00 (1.57)
95% CI of LS mean	(72.90, 79.22)	(72.91, 79.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-4.49, 4.38)
Absolute Change at Week 8 (MMRM)		
n	112	119
LS mean (SE)	1.27 (1.21)	0.83 (1.17)
95% CI of LS mean	(-1.11, 3.65)	(-1.47, 3.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.44 (-3.76, 2.88)
Week 16 (MMRM)		
n	115	119
LS mean (SE)	75.26 (1.61)	77.20 (1.58)
95% CI of LS mean	(72.09, 78.44)	(74.09, 80.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.94 (-2.52, 6.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 16 (MMRM)		
n	111	118
LS mean (SE)	0.92 (1.30)	2.03 (1.26)
95% CI of LS mean	(-1.64, 3.48)	(-0.46, 4.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.11 (-2.46, 4.68)
Week 24 (MMRM)		
n	118	118
LS mean (SE)	75.22 (1.52)	77.84 (1.50)
95% CI of LS mean	(72.21, 78.22)	(74.88, 80.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.62 (-1.61, 6.86)
Absolute Change at Week 24 (MMRM)		
n	114	117
LS mean (SE)	0.71 (1.29)	2.73 (1.27)
95% CI of LS mean	(-1.84, 3.26)	(0.23, 5.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.02 (-1.56, 5.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52		
n	115	116
Mean (SD)	79.44 (15.42)	81.09 (16.87)
Absolute Change at Week 52		
n	111	114
Mean (SD)	4.92 (15.04)	5.59 (14.19)
Week 52 (MMRM)		
n	114	115
LS mean (SE)	79.38 (1.49)	80.90 (1.46)
95% CI of LS mean	(76.45, 82.31)	(78.02, 83.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.52 (-2.60, 5.65)
Absolute Change at Week 52 (MMRM)		
n	110	113
LS mean (SE)	4.67 (1.40)	5.64 (1.37)
95% CI of LS mean	(1.92, 7.42)	(2.94, 8.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-2.89, 4.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change through Week 52 (MMRM)		
n	114	120
LS mean (SE)	2.10 (1.11)	3.47 (1.08)
95% CI of LS mean	(-0.08, 4.28)	(1.34, 5.59)
P-value within Treatment	0.0592	0.0015
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.36 (-1.69, 4.42)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3802
Hedges' G (SE)		0.11 (0.13)
Hedges' 95% CI		(-0.14, 0.37)
Hedges' P-value		0.3792

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	37	40
Mean (SD)	78.29 (17.13)	76.90 (17.08)
Week 8 (MMRM)		
n	34	36
LS mean (SE)	79.90 (2.50)	79.66 (2.40)
95% CI of LS mean	(74.91, 84.89)	(74.87, 84.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-7.19, 6.72)
Absolute Change at Week 8 (MMRM)		
n	33	36
LS mean (SE)	0.30 (2.65)	1.96 (2.51)
95% CI of LS mean	(-4.98, 5.58)	(-3.05, 6.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.66 (-5.67, 9.00)
Week 16 (MMRM)		
n	32	36
LS mean (SE)	78.29 (2.63)	81.00 (2.49)
95% CI of LS mean	(73.05, 83.53)	(76.03, 85.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.71 (-4.56, 9.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 16 (MMRM)		
n	31	36
LS mean (SE)	-0.64 (2.70)	3.21 (2.53)
95% CI of LS mean	(-6.03, 4.76)	(-1.85, 8.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.84 (-3.61, 11.30)
Week 24 (MMRM)		
n	34	36
LS mean (SE)	81.58 (2.52)	82.09 (2.42)
95% CI of LS mean	(76.55, 86.60)	(77.26, 86.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.51 (-6.49, 7.52)
Absolute Change at Week 24 (MMRM)		
n	33	35
LS mean (SE)	2.66 (2.86)	4.34 (2.74)
95% CI of LS mean	(-3.06, 8.37)	(-1.13, 9.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.68 (-6.28, 9.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52		
n	33	35
Mean (SD)	83.91 (16.66)	85.37 (13.54)
Absolute Change at Week 52		
n	32	34
Mean (SD)	5.43 (19.14)	6.14 (17.81)
Week 52 (MMRM)		
n	32	35
LS mean (SE)	83.26 (2.68)	84.52 (2.57)
95% CI of LS mean	(77.90, 88.62)	(79.39, 89.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.26 (-6.19, 8.71)
Absolute Change at Week 52 (MMRM)		
n	31	34
LS mean (SE)	3.69 (3.32)	6.07 (3.16)
95% CI of LS mean	(-2.94, 10.31)	(-0.24, 12.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-6.81, 11.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change through Week 52 (MMRM)		
n	33	38
LS mean (SE)	1.90 (2.51)	4.54 (2.38)
95% CI of LS mean	(-3.11, 6.92)	(-0.22, 9.29)
P-value within Treatment	0.4514	0.0611
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.64 (-4.33, 9.60)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4527
Hedges' G (SE)		0.18 (0.24)
Hedges' 95% CI		(-0.29, 0.65)
Hedges' P-value		0.4504

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	71.63 (17.78)	74.72 (17.99)
Week 8 (MMRM)		
n	243	237
LS mean (SE)	72.83 (1.15)	75.09 (1.17)
95% CI of LS mean	(70.57, 75.10)	(72.80, 77.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.25 (-0.97, 5.48)
Absolute Change at Week 8 (MMRM)		
n	237	234
LS mean (SE)	0.99 (0.87)	0.18 (0.87)
95% CI of LS mean	(-0.71, 2.69)	(-1.53, 1.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.81 (-3.22, 1.61)
Week 16 (MMRM)		
n	241	231
LS mean (SE)	73.99 (1.15)	75.36 (1.17)
95% CI of LS mean	(71.73, 76.25)	(73.06, 77.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.37 (-1.86, 4.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 16 (MMRM)		
n	235	228
LS mean (SE)	2.30 (0.90)	0.58 (0.91)
95% CI of LS mean	(0.54, 4.06)	(-1.20, 2.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.72 (-4.23, 0.79)
Week 24 (MMRM)		
n	240	229
LS mean (SE)	72.26 (1.14)	76.48 (1.16)
95% CI of LS mean	(70.02, 74.51)	(74.19, 78.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.22 (1.01, 7.43)
Absolute Change at Week 24 (MMRM)		
n	234	227
LS mean (SE)	0.47 (0.89)	1.70 (0.90)
95% CI of LS mean	(-1.28, 2.23)	(-0.07, 3.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.23 (-1.27, 3.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52		
n	244	230
Mean (SD)	75.48 (18.03)	78.70 (17.93)
Absolute Change at Week 52		
n	238	227
Mean (SD)	3.90 (13.94)	4.02 (13.21)
Week 52 (MMRM)		
n	237	224
LS mean (SE)	75.38 (1.16)	78.61 (1.18)
95% CI of LS mean	(73.11, 77.65)	(76.29, 80.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.23 (-0.02, 6.48)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	3.60 (0.89)	3.86 (0.90)
95% CI of LS mean	(1.86, 5.35)	(2.09, 5.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.26 (-2.23, 2.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	2.12 (0.74)	2.05 (0.75)
95% CI of LS mean	(0.67, 3.58)	(0.57, 3.52)
P-value within Treatment	0.0043	0.0066
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-2.15, 2.00)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9424
Hedges' G (SE)		-0.01 (0.09)
Hedges' 95% CI		(-0.19, 0.17)
Hedges' P-value		0.9423

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	78	71
Mean (SD)	69.96 (19.16)	73.87 (16.52)
Week 8 (MMRM)		
n	79	68
LS mean (SE)	72.92 (1.90)	75.56 (2.04)
95% CI of LS mean	(69.16, 76.68)	(71.53, 79.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.64 (-2.89, 8.17)
Absolute Change at Week 8 (MMRM)		
n	77	67
LS mean (SE)	2.23 (1.40)	2.05 (1.49)
95% CI of LS mean	(-0.54, 4.99)	(-0.90, 5.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-4.23, 3.89)
Week 16 (MMRM)		
n	77	67
LS mean (SE)	73.35 (1.97)	75.21 (2.11)
95% CI of LS mean	(69.46, 77.24)	(71.03, 79.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.86 (-3.86, 7.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 16 (MMRM)		
n	75	66
LS mean (SE)	2.99 (1.60)	1.72 (1.71)
95% CI of LS mean	(-0.17, 6.16)	(-1.65, 5.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.27 (-5.91, 3.37)
Week 24 (MMRM)		
n	79	63
LS mean (SE)	70.23 (2.09)	75.50 (2.29)
95% CI of LS mean	(66.09, 74.37)	(70.98, 80.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.27 (-0.87, 11.41)
Absolute Change at Week 24 (MMRM)		
n	77	63
LS mean (SE)	-0.32 (1.60)	1.93 (1.75)
95% CI of LS mean	(-3.48, 2.84)	(-1.53, 5.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.25 (-2.45, 6.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52		
n	78	67
Mean (SD)	76.50 (20.79)	78.86 (18.43)
Absolute Change at Week 52		
n	76	66
Mean (SD)	6.34 (13.63)	4.63 (13.45)
Week 52 (MMRM)		
n	77	64
LS mean (SE)	77.02 (2.19)	78.14 (2.37)
95% CI of LS mean	(72.69, 81.35)	(73.46, 82.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.13 (-5.27, 7.52)
Absolute Change at Week 52 (MMRM)		
n	75	63
LS mean (SE)	6.57 (1.59)	4.65 (1.72)
95% CI of LS mean	(3.43, 9.70)	(1.25, 8.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.91 (-6.55, 2.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change through Week 52 (MMRM)		
n	77	66
LS mean (SE)	3.08 (1.31)	2.77 (1.41)
95% CI of LS mean	(0.48, 5.68)	(-0.03, 5.56)
P-value within Treatment	0.0204	0.0526
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-4.14, 3.52)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8719
Hedges' G (SE)		-0.03 (0.17)
Hedges' 95% CI		(-0.36, 0.30)
Hedges' P-value		0.8714

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	197	207
Mean (SD)	73.72 (17.18)	75.35 (18.30)
Week 8 (MMRM)		
n	198	205
LS mean (SE)	74.17 (1.26)	75.68 (1.23)
95% CI of LS mean	(71.70, 76.64)	(73.26, 78.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.51 (-1.95, 4.98)
Absolute Change at Week 8 (MMRM)		
n	193	203
LS mean (SE)	0.33 (1.02)	-0.06 (0.99)
95% CI of LS mean	(-1.67, 2.33)	(-2.01, 1.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.39 (-3.19, 2.41)
Week 16 (MMRM)		
n	196	200
LS mean (SE)	75.21 (1.24)	76.38 (1.22)
95% CI of LS mean	(72.77, 77.65)	(73.97, 78.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-2.26, 4.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 16 (MMRM)		
n	191	198
LS mean (SE)	1.58 (1.01)	0.72 (0.99)
95% CI of LS mean	(-0.41, 3.57)	(-1.23, 2.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.86 (-3.65, 1.93)
Week 24 (MMRM)		
n	195	202
LS mean (SE)	74.83 (1.20)	77.71 (1.18)
95% CI of LS mean	(72.48, 77.19)	(75.40, 80.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.88 (-0.42, 6.18)
Absolute Change at Week 24 (MMRM)		
n	190	199
LS mean (SE)	1.16 (1.02)	2.13 (0.99)
95% CI of LS mean	(-0.83, 3.16)	(0.18, 4.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-1.82, 3.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52		
n	194	196
Mean (SD)	76.45 (16.95)	79.79 (17.27)
Absolute Change at Week 52		
n	189	193
Mean (SD)	3.00 (14.97)	4.22 (14.11)
Week 52 (MMRM)		
n	192	195
LS mean (SE)	76.22 (1.20)	79.67 (1.18)
95% CI of LS mean	(73.85, 78.58)	(77.34, 82.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.45 (0.13, 6.77)
Absolute Change at Week 52 (MMRM)		
n	187	192
LS mean (SE)	2.48 (1.05)	4.02 (1.03)
95% CI of LS mean	(0.42, 4.54)	(1.99, 6.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.54 (-1.36, 4.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change through Week 52 (MMRM)		
n	193	202
LS mean (SE)	1.74 (0.86)	2.29 (0.84)
95% CI of LS mean	(0.05, 3.43)	(0.63, 3.94)
P-value within Treatment	0.0441	0.0069
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.55 (-1.82, 2.92)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6490
Hedges' G (SE)		0.05 (0.10)
Hedges' 95% CI		(-0.15, 0.24)
Hedges' P-value		0.6489

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	140	146
Mean (SD)	74.21 (17.63)	77.15 (17.89)
Week 8 (MMRM)		
n	134	143
LS mean (SE)	75.96 (1.43)	77.87 (1.38)
95% CI of LS mean	(73.14, 78.77)	(75.15, 80.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.92 (-2.02, 5.86)
Absolute Change at Week 8 (MMRM)		
n	130	141
LS mean (SE)	0.69 (1.15)	0.48 (1.11)
95% CI of LS mean	(-1.58, 2.96)	(-1.70, 2.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.21 (-3.37, 2.95)
Week 16 (MMRM)		
n	130	138
LS mean (SE)	75.18 (1.47)	78.37 (1.42)
95% CI of LS mean	(72.30, 78.07)	(75.57, 81.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.18 (-0.86, 7.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 16 (MMRM)		
n	126	136
LS mean (SE)	0.32 (1.10)	1.15 (1.07)
95% CI of LS mean	(-1.86, 2.50)	(-0.95, 3.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.83 (-2.21, 3.86)
Week 24 (MMRM)		
n	133	140
LS mean (SE)	75.03 (1.49)	78.82 (1.45)
95% CI of LS mean	(72.09, 77.97)	(75.97, 81.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.79 (-0.33, 7.91)
Absolute Change at Week 24 (MMRM)		
n	129	137
LS mean (SE)	0.13 (1.17)	1.73 (1.14)
95% CI of LS mean	(-2.18, 2.44)	(-0.51, 3.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.60 (-1.63, 4.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52		
n	139	143
Mean (SD)	77.97 (17.17)	80.57 (17.51)
Absolute Change at Week 52		
n	135	140
Mean (SD)	3.70 (16.06)	3.45 (13.95)
Week 52 (MMRM)		
n	132	139
LS mean (SE)	77.74 (1.50)	80.52 (1.46)
95% CI of LS mean	(74.79, 80.70)	(77.65, 83.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.77 (-1.37, 6.91)
Absolute Change at Week 52 (MMRM)		
n	128	136
LS mean (SE)	2.74 (1.32)	3.32 (1.28)
95% CI of LS mean	(0.15, 5.33)	(0.81, 5.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-3.04, 4.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change through Week 52 (MMRM)		
n	130	139
LS mean (SE)	1.06 (1.01)	2.07 (0.98)
95% CI of LS mean	(-0.93, 3.06)	(0.13, 4.00)
P-value within Treatment	0.2951	0.0363
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.00 (-1.79, 3.80)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4815
Hedges' G (SE)		0.09 (0.12)
Hedges' 95% CI		(-0.15, 0.33)
Hedges' P-value		0.4792

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	142	134
Mean (SD)	70.83 (17.89)	72.73 (17.57)
Week 8 (MMRM)		
n	143	130
LS mean (SE)	71.97 (1.53)	73.05 (1.60)
95% CI of LS mean	(68.95, 74.99)	(69.90, 76.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.08 (-3.31, 5.47)
Absolute Change at Week 8 (MMRM)		
n	140	129
LS mean (SE)	0.64 (1.19)	0.90 (1.23)
95% CI of LS mean	(-1.70, 2.97)	(-1.53, 3.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.26 (-3.13, 3.64)
Week 16 (MMRM)		
n	143	129
LS mean (SE)	74.31 (1.51)	73.42 (1.58)
95% CI of LS mean	(71.34, 77.29)	(70.31, 76.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.89 (-5.21, 3.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 16 (MMRM)		
n	140	128
LS mean (SE)	3.07 (1.29)	1.18 (1.34)
95% CI of LS mean	(0.54, 5.61)	(-1.45, 3.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.89 (-5.56, 1.78)
Week 24 (MMRM)		
n	141	125
LS mean (SE)	72.21 (1.48)	75.24 (1.55)
95% CI of LS mean	(69.30, 75.12)	(72.18, 78.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.03 (-1.21, 7.27)
Absolute Change at Week 24 (MMRM)		
n	138	125
LS mean (SE)	0.87 (1.26)	2.89 (1.32)
95% CI of LS mean	(-1.62, 3.35)	(0.30, 5.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.03 (-1.58, 5.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52		
n	138	122
Mean (SD)	74.99 (18.84)	78.42 (17.57)
Absolute Change at Week 52		
n	135	121
Mean (SD)	4.47 (13.06)	5.27 (13.78)
Week 52 (MMRM)		
n	137	120
LS mean (SE)	75.37 (1.53)	77.81 (1.61)
95% CI of LS mean	(72.37, 78.38)	(74.64, 80.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.43 (-1.95, 6.82)
Absolute Change at Week 52 (MMRM)		
n	134	119
LS mean (SE)	4.09 (1.15)	5.51 (1.21)
95% CI of LS mean	(1.83, 6.35)	(3.13, 7.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.42 (-1.88, 4.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change through Week 52 (MMRM)		
n	140	129
LS mean (SE)	2.68 (1.02)	3.20 (1.06)
95% CI of LS mean	(0.68, 4.68)	(1.11, 5.28)
P-value within Treatment	0.0089	0.0028
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.52 (-2.39, 3.43)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7249
Hedges' G (SE)		0.04 (0.12)
Hedges' 95% CI		(-0.20, 0.28)
Hedges' P-value		0.7233

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	102	111
Mean (SD)	71.25 (18.32)	75.98 (18.68)
Week 8 (MMRM)		
n	98	112
LS mean (SE)	73.15 (1.78)	76.92 (1.67)
95% CI of LS mean	(69.63, 76.66)	(73.64, 80.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.77 (-1.04, 8.59)
Absolute Change at Week 8 (MMRM)		
n	97	109
LS mean (SE)	1.75 (1.44)	0.50 (1.36)
95% CI of LS mean	(-1.10, 4.60)	(-2.19, 3.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.25 (-5.17, 2.67)
Week 16 (MMRM)		
n	96	108
LS mean (SE)	72.46 (1.77)	78.64 (1.67)
95% CI of LS mean	(68.96, 75.96)	(75.35, 81.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.18 (1.37, 10.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 16 (MMRM)		
n	95	105
LS mean (SE)	1.00 (1.40)	2.42 (1.33)
95% CI of LS mean	(-1.77, 3.77)	(-0.21, 5.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.42 (-2.40, 5.24)
Week 24 (MMRM)		
n	98	108
LS mean (SE)	71.08 (1.82)	78.38 (1.72)
95% CI of LS mean	(67.48, 74.67)	(74.98, 81.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.30 (2.35, 12.26)
Absolute Change at Week 24 (MMRM)		
n	97	106
LS mean (SE)	-0.27 (1.42)	2.11 (1.36)
95% CI of LS mean	(-3.07, 2.53)	(-0.56, 4.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-1.50, 6.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52		
n	101	104
Mean (SD)	76.36 (17.73)	80.73 (17.44)
Absolute Change at Week 52		
n	100	101
Mean (SD)	5.51 (13.21)	4.25 (14.09)
Week 52 (MMRM)		
n	97	104
LS mean (SE)	76.30 (1.73)	80.63 (1.64)
95% CI of LS mean	(72.89, 79.71)	(77.39, 83.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.33 (-0.38, 9.04)
Absolute Change at Week 52 (MMRM)		
n	96	101
LS mean (SE)	5.02 (1.35)	4.35 (1.31)
95% CI of LS mean	(2.34, 7.69)	(1.77, 6.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.67 (-4.38, 3.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change through Week 52 (MMRM)		
n	98	107
LS mean (SE)	1.92 (1.13)	2.96 (1.08)
95% CI of LS mean	(-0.31, 4.14)	(0.83, 5.09)
P-value within Treatment	0.0913	0.0066
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.04 (-2.04, 4.13)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5060
Hedges' G (SE)		0.09 (0.14)
Hedges' 95% CI		(-0.18, 0.37)
Hedges' P-value		0.5054

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	180	169
Mean (SD)	73.22 (17.53)	74.42 (17.31)
Week 8 (MMRM)		
n	179	161
LS mean (SE)	74.14 (1.31)	74.90 (1.37)
95% CI of LS mean	(71.57, 76.71)	(72.20, 77.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.76 (-2.97, 4.49)
Absolute Change at Week 8 (MMRM)		
n	173	161
LS mean (SE)	0.41 (1.00)	0.47 (1.04)
95% CI of LS mean	(-1.56, 2.39)	(-1.57, 2.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.06 (-2.79, 2.90)
Week 16 (MMRM)		
n	177	159
LS mean (SE)	75.84 (1.31)	74.42 (1.38)
95% CI of LS mean	(73.26, 78.41)	(71.71, 77.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.42 (-5.16, 2.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	171	159
LS mean (SE)	2.51 (1.07)	0.00 (1.11)
95% CI of LS mean	(0.41, 4.62)	(-2.18, 2.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.51 (-5.54, 0.52)
Week 24 (MMRM)		
n	176	157
LS mean (SE)	74.79 (1.27)	76.45 (1.34)
95% CI of LS mean	(72.29, 77.30)	(73.81, 79.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.65 (-1.99, 5.29)
Absolute Change at Week 24 (MMRM)		
n	170	156
LS mean (SE)	1.30 (1.07)	2.07 (1.11)
95% CI of LS mean	(-0.81, 3.40)	(-0.12, 4.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.78 (-2.27, 3.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52		
n	176	161
Mean (SD)	76.56 (18.28)	78.84 (17.61)
Absolute Change at Week 52		
n	170	160
Mean (SD)	3.25 (15.36)	4.33 (13.78)
Week 52 (MMRM)		
n	172	155
LS mean (SE)	76.43 (1.35)	78.48 (1.42)
95% CI of LS mean	(73.78, 79.09)	(75.69, 81.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.04 (-1.81, 5.90)
Absolute Change at Week 52 (MMRM)		
n	166	154
LS mean (SE)	2.84 (1.13)	4.05 (1.17)
95% CI of LS mean	(0.62, 5.06)	(1.75, 6.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.21 (-1.99, 4.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	172	161
LS mean (SE)	2.22 (0.92)	2.04 (0.95)
95% CI of LS mean	(0.41, 4.03)	(0.17, 3.92)
P-value within Treatment	0.0165	0.0330
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-2.79, 2.43)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8944
Hedges' G (SE)		-0.01 (0.11)
Hedges' 95% CI		(-0.23, 0.20)
Hedges' P-value		0.8943

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	164	152
Mean (SD)	68.29 (19.31)	72.15 (18.88)
Week 8 (MMRM)		
n	161	153
LS mean (SE)	67.63 (1.55)	73.42 (1.59)
95% CI of LS mean	(64.58, 70.69)	(70.29, 76.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.78 (1.41, 10.16)
Absolute Change at Week 8 (MMRM)		
n	158	151
LS mean (SE)	-0.10 (1.10)	1.57 (1.13)
95% CI of LS mean	(-2.27, 2.07)	(-0.65, 3.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.67 (-1.44, 4.78)
Week 16 (MMRM)		
n	158	149
LS mean (SE)	69.65 (1.57)	73.09 (1.61)
95% CI of LS mean	(66.56, 72.74)	(69.91, 76.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.44 (-0.99, 7.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 16 (MMRM)		
n	155	147
LS mean (SE)	1.95 (1.16)	1.31 (1.19)
95% CI of LS mean	(-0.34, 4.24)	(-1.04, 3.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-3.92, 2.64)
Week 24 (MMRM)		
n	156	147
LS mean (SE)	69.21 (1.60)	73.42 (1.65)
95% CI of LS mean	(66.05, 72.36)	(70.18, 76.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.22 (-0.31, 8.75)
Absolute Change at Week 24 (MMRM)		
n	153	145
LS mean (SE)	1.48 (1.18)	1.61 (1.21)
95% CI of LS mean	(-0.84, 3.80)	(-0.77, 3.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-3.20, 3.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13JAN2025 12:11

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52		
n	159	145
Mean (SD)	70.93 (20.23)	74.41 (19.66)
Absolute Change at Week 52		
n	156	143
Mean (SD)	3.28 (16.85)	2.87 (14.37)
Week 52 (MMRM)		
n	155	144
LS mean (SE)	70.88 (1.58)	74.19 (1.63)
95% CI of LS mean	(67.77, 73.99)	(70.99, 77.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.31 (-1.16, 7.78)
Absolute Change at Week 52 (MMRM)		
n	152	142
LS mean (SE)	3.26 (1.28)	2.53 (1.32)
95% CI of LS mean	(0.74, 5.77)	(-0.06, 5.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.72 (-4.33, 2.89)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	2.23 (1.02)	1.82 (1.05)
95% CI of LS mean	(0.22, 4.24)	(-0.24, 3.88)
P-value within Treatment	0.0296	0.0834
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.41 (-3.29, 2.47)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7782
Hedges' G (SE)		-0.03 (0.11)
Hedges' 95% CI		(-0.26, 0.19)
Hedges' P-value		0.7781

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	115	123
Mean (SD)	72.85 (20.14)	71.45 (19.41)
Week 8 (MMRM)		
n	116	120
LS mean (SE)	74.84 (1.87)	73.63 (1.83)
95% CI of LS mean	(71.15, 78.53)	(70.03, 77.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.21 (-6.38, 3.97)
Absolute Change at Week 8 (MMRM)		
n	112	119
LS mean (SE)	2.06 (1.29)	2.06 (1.25)
95% CI of LS mean	(-0.47, 4.59)	(-0.40, 4.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-3.54, 3.53)
Week 16 (MMRM)		
n	115	119
LS mean (SE)	74.58 (1.81)	73.85 (1.77)
95% CI of LS mean	(71.01, 78.15)	(70.36, 77.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.73 (-5.74, 4.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 16 (MMRM)		
n	111	118
LS mean (SE)	1.96 (1.33)	2.13 (1.29)
95% CI of LS mean	(-0.67, 4.59)	(-0.42, 4.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-3.50, 3.83)
Week 24 (MMRM)		
n	118	118
LS mean (SE)	72.59 (1.85)	74.13 (1.83)
95% CI of LS mean	(68.94, 76.24)	(70.53, 77.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.54 (-3.60, 6.68)
Absolute Change at Week 24 (MMRM)		
n	114	117
LS mean (SE)	0.20 (1.37)	2.42 (1.34)
95% CI of LS mean	(-2.50, 2.90)	(-0.22, 5.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.22 (-1.56, 6.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52		
n	115	116
Mean (SD)	76.81 (19.05)	77.68 (19.08)
Absolute Change at Week 52		
n	111	114
Mean (SD)	3.70 (16.30)	5.95 (16.27)
Week 52 (MMRM)		
n	114	115
LS mean (SE)	76.53 (1.77)	77.88 (1.74)
95% CI of LS mean	(73.05, 80.01)	(74.45, 81.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.35 (-3.55, 6.25)
Absolute Change at Week 52 (MMRM)		
n	110	113
LS mean (SE)	3.88 (1.54)	6.01 (1.52)
95% CI of LS mean	(0.84, 6.93)	(3.03, 9.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.13 (-2.14, 6.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change through Week 52 (MMRM)		
n	114	120
LS mean (SE)	2.01 (1.19)	3.52 (1.16)
95% CI of LS mean	(-0.34, 4.37)	(1.23, 5.81)
P-value within Treatment	0.0931	0.0028
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.51 (-1.79, 4.80)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3690
Hedges' G (SE)		0.12 (0.13)
Hedges' 95% CI		(-0.14, 0.37)
Hedges' P-value		0.3681

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	37	40
Mean (SD)	72.07 (18.82)	76.11 (17.89)
Week 8 (MMRM)		
n	34	36
LS mean (SE)	79.33 (2.95)	76.97 (2.84)
95% CI of LS mean	(73.43, 85.22)	(71.31, 82.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.36 (-10.58, 5.86)
Absolute Change at Week 8 (MMRM)		
n	33	36
LS mean (SE)	7.43 (2.57)	0.20 (2.44)
95% CI of LS mean	(2.30, 12.57)	(-4.68, 5.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.23 (-14.36, -0.10)
Week 16 (MMRM)		
n	32	36
LS mean (SE)	77.60 (3.12)	76.70 (2.95)
95% CI of LS mean	(71.36, 83.83)	(70.81, 82.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.89 (-9.54, 7.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 16 (MMRM)		
n	31	36
LS mean (SE)	6.27 (2.84)	-0.25 (2.66)
95% CI of LS mean	(0.57, 11.96)	(-5.57, 5.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.51 (-14.37, 1.34)
Week 24 (MMRM)		
n	34	36
LS mean (SE)	72.95 (3.42)	75.82 (3.28)
95% CI of LS mean	(66.13, 79.78)	(69.27, 82.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.87 (-6.64, 12.37)
Absolute Change at Week 24 (MMRM)		
n	33	35
LS mean (SE)	1.97 (3.16)	-1.40 (3.04)
95% CI of LS mean	(-4.34, 8.29)	(-7.47, 4.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.37 (-12.17, 5.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52		
n	33	35
Mean (SD)	79.80 (18.31)	80.63 (16.69)
Absolute Change at Week 52		
n	32	34
Mean (SD)	7.64 (19.84)	2.29 (19.87)
Week 52 (MMRM)		
n	32	35
LS mean (SE)	78.56 (3.15)	80.05 (3.00)
95% CI of LS mean	(72.27, 84.84)	(74.05, 86.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.49 (-7.24, 10.23)
Absolute Change at Week 52 (MMRM)		
n	31	34
LS mean (SE)	7.25 (3.50)	2.47 (3.33)
95% CI of LS mean	(0.26, 14.23)	(-4.17, 9.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.78 (-14.45, 4.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change through Week 52 (MMRM)		
n	33	38
LS mean (SE)	5.16 (2.60)	0.28 (2.46)
95% CI of LS mean	(-0.04, 10.36)	(-4.65, 5.20)
P-value within Treatment	0.0516	0.9113
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.89 (-12.10, 2.33)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1806
Hedges' G (SE)		-0.32 (0.24)
Hedges' 95% CI		(-0.79, 0.15)
Hedges' P-value		0.1803

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	70.07 (19.89)	70.93 (19.19)
Week 8 (MMRM)		
n	243	237
LS mean (SE)	69.48 (1.30)	72.90 (1.32)
95% CI of LS mean	(66.92, 72.04)	(70.31, 75.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.42 (-0.22, 7.07)
Absolute Change at Week 8 (MMRM)		
n	237	234
LS mean (SE)	-0.12 (0.88)	2.02 (0.88)
95% CI of LS mean	(-1.84, 1.60)	(0.29, 3.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.14 (-0.30, 4.59)
Week 16 (MMRM)		
n	241	232
LS mean (SE)	70.91 (1.28)	72.83 (1.30)
95% CI of LS mean	(68.39, 73.43)	(70.27, 75.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.91 (-1.68, 5.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 16 (MMRM)		
n	235	229
LS mean (SE)	1.34 (0.90)	2.02 (0.91)
95% CI of LS mean	(-0.43, 3.12)	(0.22, 3.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.67 (-1.85, 3.20)
Week 24 (MMRM)		
n	240	229
LS mean (SE)	70.28 (1.30)	73.33 (1.32)
95% CI of LS mean	(67.72, 72.83)	(70.73, 75.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.05 (-0.60, 6.70)
Absolute Change at Week 24 (MMRM)		
n	234	227
LS mean (SE)	0.75 (0.92)	2.50 (0.93)
95% CI of LS mean	(-1.05, 2.55)	(0.68, 4.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.75 (-0.81, 4.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52		
n	244	230
Mean (SD)	72.63 (20.02)	75.22 (19.63)
Absolute Change at Week 52		
n	238	227
Mean (SD)	2.80 (16.06)	4.70 (14.47)
Week 52 (MMRM)		
n	237	224
LS mean (SE)	72.52 (1.28)	75.04 (1.30)
95% CI of LS mean	(70.01, 75.03)	(72.48, 77.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.52 (-1.07, 6.12)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	2.91 (1.01)	4.33 (1.03)
95% CI of LS mean	(0.93, 4.90)	(2.31, 6.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.42 (-1.41, 4.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	1.67 (0.80)	2.95 (0.81)
95% CI of LS mean	(0.10, 3.24)	(1.36, 4.54)
P-value within Treatment	0.0373	0.0003
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.28 (-0.96, 3.52)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2608
Hedges' G (SE)		0.10 (0.09)
Hedges' 95% CI		(-0.08, 0.29)
Hedges' P-value		0.2605

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	78	71
Mean (SD)	69.23 (20.57)	71.99 (20.82)
Week 8 (MMRM)		
n	79	68
LS mean (SE)	69.08 (2.42)	75.18 (2.60)
95% CI of LS mean	(64.28, 73.87)	(70.04, 80.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.11 (-0.94, 13.15)
Absolute Change at Week 8 (MMRM)		
n	77	67
LS mean (SE)	-0.03 (1.60)	3.17 (1.70)
95% CI of LS mean	(-3.19, 3.12)	(-0.20, 6.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.20 (-1.43, 7.83)
Week 16 (MMRM)		
n	77	67
LS mean (SE)	71.52 (2.35)	74.12 (2.52)
95% CI of LS mean	(66.88, 76.16)	(69.15, 79.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.60 (-4.22, 9.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 16 (MMRM)		
n	75	66
LS mean (SE)	2.06 (1.70)	1.99 (1.82)
95% CI of LS mean	(-1.30, 5.43)	(-1.60, 5.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-5.01, 4.86)
Week 24 (MMRM)		
n	79	63
LS mean (SE)	70.06 (2.44)	74.51 (2.65)
95% CI of LS mean	(65.23, 74.89)	(69.26, 79.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.45 (-2.70, 11.60)
Absolute Change at Week 24 (MMRM)		
n	77	63
LS mean (SE)	1.27 (1.70)	2.49 (1.86)
95% CI of LS mean	(-2.10, 4.64)	(-1.19, 6.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.22 (-3.78, 6.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52		
n	78	67
Mean (SD)	74.07 (20.86)	75.95 (19.88)
Absolute Change at Week 52		
n	76	66
Mean (SD)	4.68 (16.46)	4.88 (15.97)
Week 52 (MMRM)		
n	77	64
LS mean (SE)	73.88 (2.30)	75.89 (2.48)
95% CI of LS mean	(69.34, 78.41)	(70.99, 80.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.01 (-4.68, 8.71)
Absolute Change at Week 52 (MMRM)		
n	75	63
LS mean (SE)	4.56 (1.87)	3.88 (2.02)
95% CI of LS mean	(0.87, 8.25)	(-0.11, 7.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.68 (-6.13, 4.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change through Week 52 (MMRM)		
n	77	66
LS mean (SE)	2.63 (1.54)	2.78 (1.65)
95% CI of LS mean	(-0.41, 5.67)	(-0.49, 6.06)
P-value within Treatment	0.0895	0.0946
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-4.33, 4.64)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9454
Hedges' G (SE)		0.01 (0.17)
Hedges' 95% CI		(-0.32, 0.34)
Hedges' P-value		0.9452

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	197	207
Mean (SD)	70.33 (19.43)	71.44 (18.46)
Week 8 (MMRM)		
n	198	205
LS mean (SE)	71.47 (1.38)	72.83 (1.35)
95% CI of LS mean	(68.76, 74.18)	(70.17, 75.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.36 (-2.44, 5.16)
Absolute Change at Week 8 (MMRM)		
n	193	203
LS mean (SE)	1.21 (0.99)	1.26 (0.97)
95% CI of LS mean	(-0.74, 3.15)	(-0.64, 3.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-2.67, 2.77)
Week 16 (MMRM)		
n	196	201
LS mean (SE)	71.99 (1.38)	73.05 (1.36)
95% CI of LS mean	(69.27, 74.70)	(70.38, 75.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.06 (-2.74, 4.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 16 (MMRM)		
n	191	199
LS mean (SE)	1.97 (1.02)	1.52 (0.99)
95% CI of LS mean	(-0.03, 3.97)	(-0.44, 3.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.45 (-3.25, 2.35)
Week 24 (MMRM)		
n	195	202
LS mean (SE)	70.99 (1.40)	73.33 (1.37)
95% CI of LS mean	(68.24, 73.74)	(70.64, 76.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.34 (-1.51, 6.20)
Absolute Change at Week 24 (MMRM)		
n	190	199
LS mean (SE)	0.82 (1.05)	1.75 (1.03)
95% CI of LS mean	(-1.25, 2.89)	(-0.27, 3.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (-1.97, 3.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52		
n	194	196
Mean (SD)	73.14 (19.74)	75.85 (19.20)
Absolute Change at Week 52		
n	189	193
Mean (SD)	2.94 (16.82)	4.26 (15.12)
Week 52 (MMRM)		
n	192	195
LS mean (SE)	73.16 (1.38)	75.66 (1.36)
95% CI of LS mean	(70.44, 75.88)	(72.98, 78.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.50 (-1.32, 6.32)
Absolute Change at Week 52 (MMRM)		
n	187	192
LS mean (SE)	3.11 (1.16)	4.10 (1.15)
95% CI of LS mean	(0.82, 5.40)	(1.85, 6.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.99 (-2.22, 4.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change through Week 52 (MMRM)		
n	193	202
LS mean (SE)	1.97 (0.90)	2.46 (0.88)
95% CI of LS mean	(0.20, 3.73)	(0.73, 4.18)
P-value within Treatment	0.0291	0.0054
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.49 (-1.98, 2.96)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6978
Hedges' G (SE)		0.04 (0.10)
Hedges' 95% CI		(-0.16, 0.24)
Hedges' P-value		0.6977

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	140	146
Mean (SD)	71.90 (19.52)	72.75 (19.97)
Week 8 (MMRM)		
n	134	143
LS mean (SE)	72.65 (1.72)	75.41 (1.66)
95% CI of LS mean	(69.27, 76.02)	(72.14, 78.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.76 (-1.97, 7.49)
Absolute Change at Week 8 (MMRM)		
n	130	141
LS mean (SE)	1.57 (1.21)	2.54 (1.17)
95% CI of LS mean	(-0.82, 3.96)	(0.24, 4.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-2.36, 4.30)
Week 16 (MMRM)		
n	130	139
LS mean (SE)	74.59 (1.75)	74.95 (1.69)
95% CI of LS mean	(71.15, 78.03)	(71.62, 78.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-4.46, 5.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 16 (MMRM)		
n	126	137
LS mean (SE)	3.46 (1.13)	2.18 (1.09)
95% CI of LS mean	(1.24, 5.69)	(0.03, 4.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.29 (-4.39, 1.82)
Week 24 (MMRM)		
n	133	140
LS mean (SE)	73.04 (1.76)	75.54 (1.71)
95% CI of LS mean	(69.57, 76.50)	(72.18, 78.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.51 (-2.36, 7.37)
Absolute Change at Week 24 (MMRM)		
n	129	137
LS mean (SE)	2.31 (1.28)	2.64 (1.24)
95% CI of LS mean	(-0.20, 4.83)	(0.21, 5.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.33 (-3.18, 3.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52		
n	139	143
Mean (SD)	76.50 (19.80)	77.23 (20.27)
Absolute Change at Week 52		
n	135	140
Mean (SD)	4.77 (16.49)	4.84 (14.61)
Week 52 (MMRM)		
n	132	139
LS mean (SE)	75.90 (1.74)	77.38 (1.69)
95% CI of LS mean	(72.47, 79.34)	(74.04, 80.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.47 (-3.34, 6.29)
Absolute Change at Week 52 (MMRM)		
n	128	136
LS mean (SE)	5.00 (1.39)	4.56 (1.35)
95% CI of LS mean	(2.26, 7.74)	(1.91, 7.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.43 (-4.26, 3.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change through Week 52 (MMRM)		
n	130	139
LS mean (SE)	3.59 (1.05)	3.13 (1.01)
95% CI of LS mean	(1.53, 5.66)	(1.13, 5.12)
P-value within Treatment	0.0007	0.0023
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.46 (-3.35, 2.42)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7524
Hedges' G (SE)		-0.04 (0.12)
Hedges' 95% CI		(-0.28, 0.20)
Hedges' P-value		0.7511

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	142	134
Mean (SD)	68.78 (19.89)	70.48 (18.03)
Week 8 (MMRM)		
n	143	130
LS mean (SE)	69.12 (1.68)	71.10 (1.75)
95% CI of LS mean	(65.81, 72.43)	(67.65, 74.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.98 (-2.83, 6.79)
Absolute Change at Week 8 (MMRM)		
n	140	129
LS mean (SE)	0.15 (1.19)	0.90 (1.23)
95% CI of LS mean	(-2.19, 2.48)	(-1.52, 3.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.75 (-2.63, 4.14)
Week 16 (MMRM)		
n	143	129
LS mean (SE)	69.39 (1.61)	71.41 (1.69)
95% CI of LS mean	(66.21, 72.57)	(68.09, 74.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.02 (-2.61, 6.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 16 (MMRM)		
n	140	128
LS mean (SE)	0.62 (1.34)	1.15 (1.39)
95% CI of LS mean	(-2.01, 3.26)	(-1.60, 3.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.52 (-3.30, 4.34)
Week 24 (MMRM)		
n	141	125
LS mean (SE)	68.68 (1.66)	71.40 (1.74)
95% CI of LS mean	(65.40, 71.95)	(67.97, 74.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.72 (-2.05, 7.50)
Absolute Change at Week 24 (MMRM)		
n	138	125
LS mean (SE)	-0.35 (1.26)	1.25 (1.31)
95% CI of LS mean	(-2.83, 2.13)	(-1.34, 3.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.60 (-2.00, 5.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52		
n	138	122
Mean (SD)	70.45 (19.66)	74.41 (18.12)
Absolute Change at Week 52		
n	135	121
Mean (SD)	1.98 (16.62)	3.86 (16.02)
Week 52 (MMRM)		
n	137	120
LS mean (SE)	71.08 (1.59)	73.77 (1.68)
95% CI of LS mean	(67.94, 74.21)	(70.47, 77.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.69 (-1.89, 7.27)
Absolute Change at Week 52 (MMRM)		
n	134	119
LS mean (SE)	2.11 (1.41)	3.55 (1.48)
95% CI of LS mean	(-0.66, 4.88)	(0.64, 6.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.44 (-2.59, 5.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change through Week 52 (MMRM)		
n	140	129
LS mean (SE)	0.79 (1.15)	1.98 (1.20)
95% CI of LS mean	(-1.47, 3.06)	(-0.37, 4.34)
P-value within Treatment	0.4899	0.0990
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.19 (-2.10, 4.47)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4776
Hedges' G (SE)		0.09 (0.12)
Hedges' 95% CI		(-0.15, 0.33)
Hedges' P-value		0.4752

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	102	111
Mean (SD)	70.92 (19.59)	72.37 (18.22)
Week 8 (MMRM)		
n	98	112
LS mean (SE)	70.52 (2.10)	73.42 (1.97)
95% CI of LS mean	(66.37, 74.66)	(69.54, 77.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.90 (-2.79, 8.58)
Absolute Change at Week 8 (MMRM)		
n	97	109
LS mean (SE)	-0.01 (1.15)	0.85 (1.08)
95% CI of LS mean	(-2.27, 2.24)	(-1.28, 2.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.86 (-2.25, 3.97)
Week 16 (MMRM)		
n	96	108
LS mean (SE)	70.36 (2.04)	73.17 (1.91)
95% CI of LS mean	(66.35, 74.38)	(69.41, 76.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.81 (-2.70, 8.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 16 (MMRM)		
n	95	105
LS mean (SE)	0.00 (1.13)	0.49 (1.07)
95% CI of LS mean	(-2.23, 2.23)	(-1.63, 2.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.49 (-2.59, 3.57)
Week 24 (MMRM)		
n	98	108
LS mean (SE)	70.70 (2.03)	73.54 (1.91)
95% CI of LS mean	(66.70, 74.70)	(69.77, 77.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.84 (-2.67, 8.35)
Absolute Change at Week 24 (MMRM)		
n	97	106
LS mean (SE)	0.42 (1.38)	0.73 (1.32)
95% CI of LS mean	(-2.30, 3.13)	(-1.86, 3.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.31 (-3.45, 4.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52		
n	101	104
Mean (SD)	70.63 (21.12)	76.28 (18.90)
Absolute Change at Week 52		
n	100	101
Mean (SD)	0.11 (17.41)	3.52 (13.23)
Week 52 (MMRM)		
n	97	104
LS mean (SE)	70.63 (2.02)	76.22 (1.92)
95% CI of LS mean	(66.65, 74.61)	(72.44, 80.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.59 (0.09, 11.09)
Absolute Change at Week 52 (MMRM)		
n	96	101
LS mean (SE)	0.54 (1.58)	3.62 (1.53)
95% CI of LS mean	(-2.59, 3.66)	(0.60, 6.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.08 (-1.27, 7.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change through Week 52 (MMRM)		
n	98	107
LS mean (SE)	0.32 (1.12)	1.61 (1.07)
95% CI of LS mean	(-1.88, 2.52)	(-0.49, 3.72)
P-value within Treatment	0.7764	0.1322
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.30 (-1.75, 4.34)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4029
Hedges' G (SE)		0.12 (0.14)
Hedges' 95% CI		(-0.16, 0.39)
Hedges' P-value		0.4026

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	180	169
Mean (SD)	70.00 (19.86)	71.20 (19.64)
Week 8 (MMRM)		
n	179	161
LS mean (SE)	70.77 (1.46)	73.59 (1.53)
95% CI of LS mean	(67.91, 73.64)	(70.58, 76.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.82 (-1.34, 6.98)
Absolute Change at Week 8 (MMRM)		
n	173	161
LS mean (SE)	1.25 (1.16)	2.39 (1.20)
95% CI of LS mean	(-1.02, 3.53)	(0.03, 4.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.14 (-2.14, 4.42)
Week 16 (MMRM)		
n	177	160
LS mean (SE)	72.50 (1.46)	73.61 (1.53)
95% CI of LS mean	(69.64, 75.37)	(70.60, 76.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.11 (-3.05, 5.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	171	160
LS mean (SE)	3.04 (1.22)	2.43 (1.26)
95% CI of LS mean	(0.64, 5.45)	(-0.05, 4.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.61 (-4.08, 2.85)
Week 24 (MMRM)		
n	176	157
LS mean (SE)	70.58 (1.52)	73.88 (1.60)
95% CI of LS mean	(67.59, 73.58)	(70.73, 77.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.30 (-1.06, 7.65)
Absolute Change at Week 24 (MMRM)		
n	170	156
LS mean (SE)	1.19 (1.17)	2.83 (1.21)
95% CI of LS mean	(-1.10, 3.49)	(0.44, 5.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.63 (-1.68, 4.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52		
n	176	161
Mean (SD)	75.13 (19.08)	75.71 (19.65)
Absolute Change at Week 52		
n	170	160
Mean (SD)	5.29 (15.82)	4.93 (16.43)
Week 52 (MMRM)		
n	172	155
LS mean (SE)	74.76 (1.45)	75.55 (1.52)
95% CI of LS mean	(71.91, 77.61)	(72.55, 78.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.79 (-3.35, 4.93)
Absolute Change at Week 52 (MMRM)		
n	166	154
LS mean (SE)	5.21 (1.25)	4.41 (1.30)
95% CI of LS mean	(2.74, 7.67)	(1.85, 6.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.80 (-4.35, 2.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	172	161
LS mean (SE)	3.15 (1.04)	3.22 (1.08)
95% CI of LS mean	(1.10, 5.20)	(1.10, 5.35)
P-value within Treatment	0.0027	0.0030
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-2.88, 3.03)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9609
Hedges' G (SE)		0.01 (0.11)
Hedges' 95% CI		(-0.21, 0.22)
Hedges' P-value		0.9608

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	163	152
Mean (SD)	65.44 (19.43)	67.38 (19.28)
Week 8 (MMRM)		
n	161	153
LS mean (SE)	61.53 (1.69)	66.57 (1.73)
95% CI of LS mean	(58.21, 64.85)	(63.16, 69.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.03 (0.27, 9.79)
Absolute Change at Week 8 (MMRM)		
n	158	151
LS mean (SE)	-3.30 (1.35)	-0.75 (1.38)
95% CI of LS mean	(-5.95, -0.64)	(-3.46, 1.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.55 (-1.25, 6.35)
Week 16 (MMRM)		
n	158	149
LS mean (SE)	61.88 (1.65)	65.51 (1.70)
95% CI of LS mean	(58.63, 65.13)	(62.17, 68.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.63 (-1.03, 8.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 16 (MMRM)		
n	155	147
LS mean (SE)	-2.77 (1.28)	-1.78 (1.31)
95% CI of LS mean	(-5.28, -0.25)	(-4.36, 0.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.99 (-2.62, 4.59)
Week 24 (MMRM)		
n	155	147
LS mean (SE)	59.96 (1.78)	65.23 (1.83)
95% CI of LS mean	(56.45, 63.46)	(61.63, 68.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.27 (0.24, 10.29)
Absolute Change at Week 24 (MMRM)		
n	152	145
LS mean (SE)	-5.09 (1.41)	-1.94 (1.44)
95% CI of LS mean	(-7.86, -2.32)	(-4.78, 0.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.15 (-0.82, 7.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52		
n	159	145
Mean (SD)	62.11 (21.33)	67.64 (19.46)
Absolute Change at Week 52		
n	156	143
Mean (SD)	-2.72 (16.40)	0.35 (14.76)
Week 52 (MMRM)		
n	155	144
LS mean (SE)	61.76 (1.60)	67.09 (1.65)
95% CI of LS mean	(58.60, 64.92)	(63.83, 70.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.32 (0.78, 9.86)
Absolute Change at Week 52 (MMRM)		
n	152	142
LS mean (SE)	-3.09 (1.28)	0.05 (1.32)
95% CI of LS mean	(-5.60, -0.57)	(-2.55, 2.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.13 (-0.49, 6.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	-3.65 (1.05)	-1.22 (1.08)
95% CI of LS mean	(-5.72, -1.58)	(-3.35, 0.90)
P-value within Treatment	0.0006	0.2584
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.42 (-0.55, 5.40)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1095
Hedges' G (SE)		0.18 (0.11)
Hedges' 95% CI		(-0.04, 0.41)
Hedges' P-value		0.1099

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	103	109
Mean (SD)	68.69 (18.54)	66.36 (18.56)
Week 8 (MMRM)		
n	105	108
LS mean (SE)	67.80 (1.85)	66.24 (1.83)
95% CI of LS mean	(64.14, 71.45)	(62.63, 69.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.56 (-6.71, 3.60)
Absolute Change at Week 8 (MMRM)		
n	103	107
LS mean (SE)	-0.87 (1.48)	-0.16 (1.45)
95% CI of LS mean	(-3.80, 2.05)	(-3.03, 2.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.71 (-3.40, 4.81)
Week 16 (MMRM)		
n	105	106
LS mean (SE)	66.89 (1.89)	65.70 (1.87)
95% CI of LS mean	(63.17, 70.61)	(62.02, 69.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.19 (-6.44, 4.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 16 (MMRM)		
n	102	105
LS mean (SE)	-1.61 (1.48)	-0.66 (1.45)
95% CI of LS mean	(-4.52, 1.31)	(-3.53, 2.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.95 (-3.15, 5.05)
Week 24 (MMRM)		
n	106	104
LS mean (SE)	67.18 (1.77)	64.02 (1.77)
95% CI of LS mean	(63.69, 70.67)	(60.53, 67.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.17 (-8.12, 1.78)
Absolute Change at Week 24 (MMRM)		
n	103	104
LS mean (SE)	-1.60 (1.61)	-2.59 (1.60)
95% CI of LS mean	(-4.78, 1.58)	(-5.73, 0.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.99 (-5.48, 3.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52		
n	104	102
Mean (SD)	68.99 (16.97)	67.32 (16.98)
Absolute Change at Week 52		
n	101	101
Mean (SD)	0.33 (15.76)	0.17 (15.41)
Week 52 (MMRM)		
n	104	101
LS mean (SE)	68.82 (1.68)	66.66 (1.69)
95% CI of LS mean	(65.50, 72.14)	(63.34, 69.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.16 (-6.88, 2.56)
Absolute Change at Week 52 (MMRM)		
n	101	100
LS mean (SE)	0.25 (1.57)	0.01 (1.56)
95% CI of LS mean	(-2.85, 3.34)	(-3.07, 3.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-4.61, 4.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change through Week 52 (MMRM)		
n	103	106
LS mean (SE)	-0.99 (1.28)	-1.08 (1.26)
95% CI of LS mean	(-3.51, 1.54)	(-3.57, 1.41)
P-value within Treatment	0.4413	0.3927
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-3.65, 3.46)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9589
Hedges' G (SE)		-0.01 (0.14)
Hedges' 95% CI		(-0.28, 0.26)
Hedges' P-value		0.9588

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	24	26
Mean (SD)	76.74 (18.87)	62.82 (22.01)
Week 8 (MMRM)		
n	24	24
LS mean (SE)	75.80 (4.08)	66.39 (4.02)
95% CI of LS mean	(67.54, 84.05)	(58.27, 74.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.41 (-21.19, 2.38)
Absolute Change at Week 8 (MMRM)		
n	24	24
LS mean (SE)	-1.44 (3.17)	3.97 (3.13)
95% CI of LS mean	(-7.83, 4.94)	(-2.34, 10.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.42 (-3.73, 14.56)
Week 16 (MMRM)		
n	22	23
LS mean (SE)	74.34 (4.11)	66.10 (4.03)
95% CI of LS mean	(66.05, 82.64)	(57.96, 74.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.24 (-20.07, 3.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 16 (MMRM)		
n	22	23
LS mean (SE)	-2.13 (3.16)	3.60 (3.12)
95% CI of LS mean	(-8.52, 4.26)	(-2.70, 9.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.73 (-3.41, 14.88)
Week 24 (MMRM)		
n	22	22
LS mean (SE)	74.35 (3.70)	67.73 (3.66)
95% CI of LS mean	(66.85, 81.85)	(60.33, 75.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.62 (-17.37, 4.14)
Absolute Change at Week 24 (MMRM)		
n	22	22
LS mean (SE)	-2.74 (3.40)	4.11 (3.37)
95% CI of LS mean	(-9.63, 4.15)	(-2.71, 10.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.85 (-2.99, 16.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52		
n	22	21
Mean (SD)	75.38 (17.91)	71.83 (16.77)
Absolute Change at Week 52		
n	22	21
Mean (SD)	-0.38 (17.34)	3.57 (16.79)
Week 52 (MMRM)		
n	22	21
LS mean (SE)	74.40 (4.04)	67.73 (4.06)
95% CI of LS mean	(66.20, 82.61)	(59.52, 75.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.68 (-18.49, 5.14)
Absolute Change at Week 52 (MMRM)		
n	22	21
LS mean (SE)	-2.62 (3.79)	4.37 (3.82)
95% CI of LS mean	(-10.33, 5.09)	(-3.36, 12.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.99 (-4.06, 18.04)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change through Week 52 (MMRM)		
n	22	24
LS mean (SE)	-2.50 (2.91)	4.03 (2.88)
95% CI of LS mean	(-8.40, 3.40)	(-1.80, 9.86)
P-value within Treatment	0.3960	0.1699
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.52 (-1.95, 15.00)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1272
Hedges' G (SE)		0.46 (0.29)
Hedges' 95% CI		(-0.13, 1.05)
Hedges' P-value		0.1231

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	65.78 (18.81)	67.26 (18.53)
Week 8 (MMRM)		
n	242	237
LS mean (SE)	62.79 (1.31)	66.48 (1.33)
95% CI of LS mean	(60.21, 65.37)	(63.87, 69.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.69 (0.01, 7.36)
Absolute Change at Week 8 (MMRM)		
n	237	234
LS mean (SE)	-2.53 (1.06)	-0.90 (1.06)
95% CI of LS mean	(-4.61, -0.45)	(-2.99, 1.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.63 (-1.32, 4.58)
Week 16 (MMRM)		
n	241	232
LS mean (SE)	62.77 (1.30)	65.57 (1.32)
95% CI of LS mean	(60.21, 65.33)	(62.97, 68.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.80 (-0.85, 6.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 16 (MMRM)		
n	235	229
LS mean (SE)	-2.46 (1.02)	-1.70 (1.03)
95% CI of LS mean	(-4.45, -0.46)	(-3.73, 0.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.75 (-2.09, 3.60)
Week 24 (MMRM)		
n	239	229
LS mean (SE)	61.65 (1.36)	64.45 (1.38)
95% CI of LS mean	(58.99, 64.31)	(61.74, 67.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.80 (-1.00, 6.60)
Absolute Change at Week 24 (MMRM)		
n	233	227
LS mean (SE)	-3.96 (1.12)	-2.77 (1.13)
95% CI of LS mean	(-6.15, -1.76)	(-4.99, -0.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.19 (-1.94, 4.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52		
n	244	230
Mean (SD)	64.00 (19.88)	67.28 (18.57)
Absolute Change at Week 52		
n	238	227
Mean (SD)	-1.58 (16.19)	0.26 (14.96)
Week 52 (MMRM)		
n	237	224
LS mean (SE)	63.53 (1.23)	66.81 (1.26)
95% CI of LS mean	(61.11, 65.95)	(64.33, 69.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.27 (-0.19, 6.74)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	-1.84 (1.03)	-0.31 (1.05)
95% CI of LS mean	(-3.86, 0.18)	(-2.37, 1.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.53 (-1.36, 4.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	-2.75 (0.85)	-1.59 (0.86)
95% CI of LS mean	(-4.41, -1.08)	(-3.28, 0.09)
P-value within Treatment	0.0013	0.0641
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.16 (-1.22, 3.53)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3388
Hedges' G (SE)		0.09 (0.09)
Hedges' 95% CI		(-0.09, 0.27)
Hedges' P-value		0.3384

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	77	70
Mean (SD)	64.72 (19.21)	67.38 (20.94)
Week 8 (MMRM)		
n	78	68
LS mean (SE)	63.05 (2.17)	67.01 (2.33)
95% CI of LS mean	(58.76, 67.35)	(62.41, 71.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.96 (-2.35, 10.27)
Absolute Change at Week 8 (MMRM)		
n	76	67
LS mean (SE)	-1.76 (1.69)	-0.12 (1.80)
95% CI of LS mean	(-5.10, 1.58)	(-3.68, 3.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.64 (-3.26, 6.54)
Week 16 (MMRM)		
n	77	66
LS mean (SE)	62.78 (2.29)	63.86 (2.47)
95% CI of LS mean	(58.25, 67.32)	(58.98, 68.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.08 (-5.60, 7.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 16 (MMRM)		
n	75	65
LS mean (SE)	-1.43 (1.72)	-3.21 (1.84)
95% CI of LS mean	(-4.83, 1.97)	(-6.85, 0.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.78 (-6.78, 3.22)
Week 24 (MMRM)		
n	77	62
LS mean (SE)	59.63 (2.43)	65.26 (2.66)
95% CI of LS mean	(54.82, 64.44)	(60.01, 70.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.63 (-1.50, 12.76)
Absolute Change at Week 24 (MMRM)		
n	75	62
LS mean (SE)	-5.31 (1.85)	-1.87 (2.02)
95% CI of LS mean	(-8.96, -1.66)	(-5.86, 2.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.44 (-1.98, 8.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52		
n	77	66
Mean (SD)	64.29 (20.18)	69.44 (19.85)
Absolute Change at Week 52		
n	75	65
Mean (SD)	-0.33 (16.29)	1.41 (17.34)
Week 52 (MMRM)		
n	76	63
LS mean (SE)	64.18 (2.28)	67.95 (2.47)
95% CI of LS mean	(59.67, 68.68)	(63.05, 72.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.77 (-2.89, 10.44)
Absolute Change at Week 52 (MMRM)		
n	74	62
LS mean (SE)	-0.59 (1.93)	0.81 (2.10)
95% CI of LS mean	(-4.41, 3.23)	(-3.34, 4.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.40 (-4.25, 7.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change through Week 52 (MMRM)		
n	76	65
LS mean (SE)	-2.44 (1.46)	-1.42 (1.58)
95% CI of LS mean	(-5.33, 0.44)	(-4.54, 1.70)
P-value within Treatment	0.0964	0.3693
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.02 (-3.24, 5.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6367
Hedges' G (SE)		0.08 (0.17)
Hedges' 95% CI		(-0.25, 0.41)
Hedges' P-value		0.6355

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	187	194
Mean (SD)	67.38 (18.74)	66.45 (18.10)
Week 8 (MMRM)		
n	188	193
LS mean (SE)	64.49 (1.52)	66.16 (1.50)
95% CI of LS mean	(61.50, 67.47)	(63.21, 69.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.67 (-2.52, 5.86)
Absolute Change at Week 8 (MMRM)		
n	185	191
LS mean (SE)	-2.58 (1.23)	-0.64 (1.21)
95% CI of LS mean	(-5.00, -0.15)	(-3.03, 1.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.93 (-1.48, 5.34)
Week 16 (MMRM)		
n	186	189
LS mean (SE)	64.39 (1.48)	66.12 (1.46)
95% CI of LS mean	(61.48, 67.29)	(63.24, 68.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.73 (-2.36, 5.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 16 (MMRM)		
n	182	187
LS mean (SE)	-2.68 (1.16)	-0.61 (1.14)
95% CI of LS mean	(-4.96, -0.40)	(-2.85, 1.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.07 (-1.13, 5.28)
Week 24 (MMRM)		
n	184	189
LS mean (SE)	64.25 (1.50)	64.43 (1.48)
95% CI of LS mean	(61.29, 67.20)	(61.52, 67.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.19 (-3.97, 4.34)
Absolute Change at Week 24 (MMRM)		
n	180	187
LS mean (SE)	-3.04 (1.28)	-2.27 (1.25)
95% CI of LS mean	(-5.55, -0.53)	(-4.74, 0.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.77 (-2.75, 4.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52		
n	185	183
Mean (SD)	64.82 (19.60)	66.89 (17.85)
Absolute Change at Week 52		
n	181	181
Mean (SD)	-2.12 (16.37)	0.28 (14.35)
Week 52 (MMRM)		
n	183	182
LS mean (SE)	64.79 (1.38)	66.45 (1.37)
95% CI of LS mean	(62.08, 67.50)	(63.75, 69.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.66 (-2.17, 5.48)
Absolute Change at Week 52 (MMRM)		
n	179	180
LS mean (SE)	-2.27 (1.15)	-0.18 (1.14)
95% CI of LS mean	(-4.52, -0.01)	(-2.42, 2.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.08 (-1.10, 5.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change through Week 52 (MMRM)		
n	183	189
LS mean (SE)	-2.66 (0.97)	-1.02 (0.95)
95% CI of LS mean	(-4.56, -0.76)	(-2.89, 0.85)
P-value within Treatment	0.0062	0.2842
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.64 (-1.03, 4.31)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2273
Hedges' G (SE)		0.13 (0.10)
Hedges' 95% CI		(-0.08, 0.33)
Hedges' P-value		0.2273

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	133	141
Mean (SD)	67.48 (18.23)	69.80 (19.30)
Week 8 (MMRM)		
n	130	139
LS mean (SE)	65.25 (1.76)	70.09 (1.70)
95% CI of LS mean	(61.79, 68.70)	(66.75, 73.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.85 (0.01, 9.68)
Absolute Change at Week 8 (MMRM)		
n	127	137
LS mean (SE)	-1.92 (1.48)	0.32 (1.43)
95% CI of LS mean	(-4.84, 0.99)	(-2.49, 3.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.25 (-1.82, 6.32)
Week 16 (MMRM)		
n	126	135
LS mean (SE)	65.65 (1.67)	70.18 (1.62)
95% CI of LS mean	(62.36, 68.94)	(67.00, 73.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.54 (-0.07, 9.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 16 (MMRM)		
n	123	133
LS mean (SE)	-1.08 (1.36)	0.57 (1.31)
95% CI of LS mean	(-3.76, 1.61)	(-2.02, 3.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.64 (-2.10, 5.38)
Week 24 (MMRM)		
n	126	134
LS mean (SE)	64.85 (1.75)	68.02 (1.70)
95% CI of LS mean	(61.40, 68.29)	(64.68, 71.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.18 (-1.65, 8.00)
Absolute Change at Week 24 (MMRM)		
n	123	132
LS mean (SE)	-2.26 (1.54)	-1.50 (1.49)
95% CI of LS mean	(-5.30, 0.78)	(-4.43, 1.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.76 (-3.48, 5.00)

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- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52		
n	132	137
Mean (SD)	65.66 (18.96)	70.50 (17.30)
Absolute Change at Week 52		
n	129	135
Mean (SD)	-1.23 (16.96)	1.05 (14.45)
Week 52 (MMRM)		
n	126	133
LS mean (SE)	65.19 (1.59)	70.21 (1.54)
95% CI of LS mean	(62.07, 68.32)	(67.17, 73.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.02 (0.63, 9.40)
Absolute Change at Week 52 (MMRM)		
n	123	131
LS mean (SE)	-1.81 (1.41)	0.81 (1.37)
95% CI of LS mean	(-4.59, 0.97)	(-1.88, 3.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.63 (-1.26, 6.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change through Week 52 (MMRM)		
n	125	134
LS mean (SE)	-1.72 (1.20)	-0.04 (1.16)
95% CI of LS mean	(-4.09, 0.65)	(-2.33, 2.25)
P-value within Treatment	0.1552	0.9726
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.68 (-1.64, 4.99)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3204
Hedges' G (SE)		0.12 (0.12)
Hedges' 95% CI		(-0.12, 0.37)
Hedges' P-value		0.3179

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- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	136	125
Mean (SD)	66.05 (19.84)	63.47 (17.92)
Week 8 (MMRM)		
n	136	122
LS mean (SE)	63.01 (1.75)	62.11 (1.85)
95% CI of LS mean	(59.56, 66.46)	(58.47, 65.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.90 (-5.95, 4.15)
Absolute Change at Week 8 (MMRM)		
n	134	121
LS mean (SE)	-2.90 (1.34)	-1.24 (1.41)
95% CI of LS mean	(-5.55, -0.26)	(-4.02, 1.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.66 (-2.19, 5.52)
Week 16 (MMRM)		
n	137	120
LS mean (SE)	62.37 (1.79)	60.23 (1.90)
95% CI of LS mean	(58.84, 65.90)	(56.47, 63.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.15 (-7.33, 3.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
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Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 16 (MMRM)		
n	134	119
LS mean (SE)	-3.63 (1.37)	-3.20 (1.44)
95% CI of LS mean	(-6.32, -0.94)	(-6.04, -0.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-3.50, 4.36)
Week 24 (MMRM)		
n	135	117
LS mean (SE)	61.12 (1.85)	60.71 (1.97)
95% CI of LS mean	(57.48, 64.76)	(56.84, 64.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.41 (-5.75, 4.93)
Absolute Change at Week 24 (MMRM)		
n	132	117
LS mean (SE)	-5.21 (1.47)	-2.79 (1.56)
95% CI of LS mean	(-8.11, -2.31)	(-5.85, 0.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.42 (-1.81, 6.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52		
n	134	114
Mean (SD)	64.24 (20.91)	64.25 (19.26)
Absolute Change at Week 52		
n	131	113
Mean (SD)	-1.72 (15.60)	-0.07 (15.92)
Week 52 (MMRM)		
n	133	112
LS mean (SE)	64.15 (1.74)	62.88 (1.86)
95% CI of LS mean	(60.73, 67.57)	(59.22, 66.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.26 (-6.30, 3.78)
Absolute Change at Week 52 (MMRM)		
n	130	111
LS mean (SE)	-1.87 (1.38)	-0.65 (1.48)
95% CI of LS mean	(-4.59, 0.85)	(-3.56, 2.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.23 (-2.77, 5.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change through Week 52 (MMRM)		
n	134	120
LS mean (SE)	-3.57 (1.09)	-2.21 (1.15)
95% CI of LS mean	(-5.72, -1.42)	(-4.48, 0.06)
P-value within Treatment	0.0012	0.0566
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.36 (-1.79, 4.51)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3955
Hedges' G (SE)		0.11 (0.13)
Hedges' 95% CI		(-0.14, 0.35)
Hedges' P-value		0.3928

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- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
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Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	99	108
Mean (SD)	64.31 (19.64)	66.59 (18.25)
Week 8 (MMRM)		
n	96	109
LS mean (SE)	61.66 (2.04)	68.23 (1.91)
95% CI of LS mean	(57.65, 65.68)	(64.47, 71.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.57 (1.06, 12.07)
Absolute Change at Week 8 (MMRM)		
n	95	106
LS mean (SE)	-1.93 (1.51)	1.66 (1.43)
95% CI of LS mean	(-4.91, 1.04)	(-1.16, 4.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.59 (-0.51, 7.69)
Week 16 (MMRM)		
n	94	105
LS mean (SE)	61.03 (2.03)	66.58 (1.91)
95% CI of LS mean	(57.03, 65.02)	(62.82, 70.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.55 (0.06, 11.04)

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Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 16 (MMRM)		
n	93	102
LS mean (SE)	-2.72 (1.50)	0.12 (1.43)
95% CI of LS mean	(-5.68, 0.24)	(-2.70, 2.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.84 (-1.26, 6.94)
Week 24 (MMRM)		
n	94	105
LS mean (SE)	60.53 (1.98)	66.65 (1.86)
95% CI of LS mean	(56.64, 64.43)	(62.98, 70.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.11 (0.76, 11.47)
Absolute Change at Week 24 (MMRM)		
n	93	103
LS mean (SE)	-3.16 (1.46)	0.33 (1.38)
95% CI of LS mean	(-6.03, -0.28)	(-2.40, 3.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.48 (-0.49, 7.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52		
n	98	101
Mean (SD)	62.59 (19.15)	67.99 (16.94)
Absolute Change at Week 52		
n	97	98
Mean (SD)	-1.37 (14.72)	1.36 (14.54)
Week 52 (MMRM)		
n	94	101
LS mean (SE)	61.79 (1.82)	67.21 (1.73)
95% CI of LS mean	(58.20, 65.37)	(63.80, 70.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.42 (0.46, 10.37)
Absolute Change at Week 52 (MMRM)		
n	93	98
LS mean (SE)	-1.76 (1.52)	0.95 (1.47)
95% CI of LS mean	(-4.75, 1.24)	(-1.94, 3.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.71 (-1.46, 6.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change through Week 52 (MMRM)		
n	95	104
LS mean (SE)	-2.54 (1.22)	0.47 (1.16)
95% CI of LS mean	(-4.94, -0.15)	(-1.82, 2.75)
P-value within Treatment	0.0377	0.6878
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.01 (-0.31, 6.33)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0753
Hedges' G (SE)		0.25 (0.14)
Hedges' 95% CI		(-0.03, 0.53)
Hedges' P-value		0.0759

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	170	158
Mean (SD)	68.19 (18.59)	66.98 (19.39)
Week 8 (MMRM)		
n	170	152
LS mean (SE)	65.29 (1.59)	65.18 (1.68)
95% CI of LS mean	(62.17, 68.41)	(61.87, 68.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-4.66, 4.44)
Absolute Change at Week 8 (MMRM)		
n	166	152
LS mean (SE)	-2.70 (1.33)	-1.88 (1.39)
95% CI of LS mean	(-5.31, -0.09)	(-4.60, 0.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.82 (-2.95, 4.60)
Week 16 (MMRM)		
n	169	150
LS mean (SE)	65.42 (1.57)	64.92 (1.67)
95% CI of LS mean	(62.33, 68.51)	(61.64, 68.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.50 (-5.01, 4.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	150
LS mean (SE)	-2.18 (1.26)	-2.16 (1.32)
95% CI of LS mean	(-4.65, 0.30)	(-4.75, 0.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.02 (-3.57, 3.61)
Week 24 (MMRM)		
n	167	146
LS mean (SE)	64.08 (1.67)	63.34 (1.78)
95% CI of LS mean	(60.80, 67.36)	(59.84, 66.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.75 (-5.55, 4.05)
Absolute Change at Week 24 (MMRM)		
n	162	146
LS mean (SE)	-4.14 (1.45)	-3.82 (1.53)
95% CI of LS mean	(-7.00, -1.29)	(-6.83, -0.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.32 (-3.83, 4.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52		
n	168	150
Mean (SD)	66.32 (20.32)	67.44 (19.44)
Absolute Change at Week 52		
n	163	150
Mean (SD)	-1.53 (17.15)	0.00 (15.51)
Week 52 (MMRM)		
n	165	144
LS mean (SE)	66.08 (1.54)	66.71 (1.64)
95% CI of LS mean	(63.06, 69.11)	(63.49, 69.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-3.80, 5.06)
Absolute Change at Week 52 (MMRM)		
n	160	144
LS mean (SE)	-1.88 (1.30)	-0.48 (1.36)
95% CI of LS mean	(-4.43, 0.67)	(-3.16, 2.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.40 (-2.31, 5.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	150
LS mean (SE)	-2.73 (1.07)	-2.15 (1.12)
95% CI of LS mean	(-4.84, -0.62)	(-4.37, 0.06)
P-value within Treatment	0.0113	0.0563
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-2.48, 3.64)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7103
Hedges' G (SE)		0.04 (0.11)
Hedges' 95% CI		(-0.18, 0.26)
Hedges' P-value		0.7098

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
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Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	160	152
Mean (SD)	90.00 (21.73)	85.31 (27.59)
Week 8 (MMRM)		
n	158	152
LS mean (SE)	86.32 (2.16)	85.54 (2.20)
95% CI of LS mean	(82.07, 90.56)	(81.21, 89.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.78 (-6.85, 5.29)
Absolute Change at Week 8 (MMRM)		
n	155	150
LS mean (SE)	-4.32 (1.65)	0.02 (1.68)
95% CI of LS mean	(-7.57, -1.06)	(-3.29, 3.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.33 (-0.31, 8.97)
Week 16 (MMRM)		
n	154	149
LS mean (SE)	83.91 (2.22)	86.18 (2.27)
95% CI of LS mean	(79.54, 88.28)	(81.72, 90.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.28 (-3.97, 8.53)

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- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 16 (MMRM)		
n	151	147
LS mean (SE)	-6.84 (1.79)	0.65 (1.81)
95% CI of LS mean	(-10.35, -3.32)	(-2.92, 4.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.48 (2.47, 12.50)
Week 24 (MMRM)		
n	153	147
LS mean (SE)	85.78 (2.16)	85.77 (2.20)
95% CI of LS mean	(81.54, 90.03)	(81.43, 90.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.01 (-6.09, 6.06)
Absolute Change at Week 24 (MMRM)		
n	150	145
LS mean (SE)	-4.71 (1.73)	0.37 (1.76)
95% CI of LS mean	(-8.12, -1.30)	(-3.09, 3.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.08 (0.22, 9.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Domain: Weight
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52		
n	159	144
Mean (SD)	86.79 (26.79)	84.49 (27.29)
Absolute Change at Week 52		
n	153	142
Mean (SD)	-3.92 (23.55)	-0.94 (19.43)
Week 52 (MMRM)		
n	155	143
LS mean (SE)	86.29 (2.15)	84.31 (2.22)
95% CI of LS mean	(82.06, 90.53)	(79.93, 88.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.98 (-8.08, 4.11)
Absolute Change at Week 52 (MMRM)		
n	149	141
LS mean (SE)	-4.37 (1.80)	-1.15 (1.85)
95% CI of LS mean	(-7.93, -0.82)	(-4.79, 2.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.22 (-1.86, 8.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change through Week 52 (MMRM)		
n	153	148
LS mean (SE)	-5.31 (1.41)	-0.04 (1.44)
95% CI of LS mean	(-8.09, -2.52)	(-2.87, 2.78)
P-value within Treatment	0.0002	0.9753
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.26 (1.29, 9.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0096
Hedges' G (SE)		0.30 (0.12)
Hedges' 95% CI		(0.07, 0.53)
Hedges' P-value		0.0099

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	103	109
Mean (SD)	86.08 (27.43)	82.87 (26.69)
Week 8 (MMRM)		
n	104	108
LS mean (SE)	88.84 (2.52)	83.86 (2.48)
95% CI of LS mean	(83.86, 93.82)	(78.97, 88.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.98 (-11.99, 2.03)
Absolute Change at Week 8 (MMRM)		
n	103	107
LS mean (SE)	2.58 (2.00)	0.77 (1.96)
95% CI of LS mean	(-1.37, 6.53)	(-3.09, 4.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.81 (-7.35, 3.74)
Week 16 (MMRM)		
n	103	106
LS mean (SE)	90.13 (2.59)	85.00 (2.56)
95% CI of LS mean	(85.03, 95.24)	(79.97, 90.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.13 (-12.33, 2.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 16 (MMRM)		
n	102	105
LS mean (SE)	3.89 (2.21)	2.12 (2.17)
95% CI of LS mean	(-0.47, 8.25)	(-2.17, 6.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.77 (-7.90, 4.35)
Week 24 (MMRM)		
n	104	104
LS mean (SE)	86.95 (2.81)	84.46 (2.78)
95% CI of LS mean	(81.42, 92.48)	(78.98, 89.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.49 (-10.30, 5.32)
Absolute Change at Week 24 (MMRM)		
n	103	104
LS mean (SE)	0.64 (1.99)	1.58 (1.97)
95% CI of LS mean	(-3.29, 4.57)	(-2.30, 5.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.95 (-4.60, 6.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52		
n	104	102
Mean (SD)	87.18 (25.99)	83.66 (29.57)
Absolute Change at Week 52		
n	101	101
Mean (SD)	0.99 (20.79)	0.99 (26.02)
Week 52 (MMRM)		
n	104	101
LS mean (SE)	87.39 (2.69)	84.08 (2.68)
95% CI of LS mean	(82.09, 92.69)	(78.79, 89.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.31 (-10.83, 4.21)
Absolute Change at Week 52 (MMRM)		
n	101	100
LS mean (SE)	1.05 (2.30)	1.31 (2.28)
95% CI of LS mean	(-3.48, 5.58)	(-3.19, 5.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.26 (-6.14, 6.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change through Week 52 (MMRM)		
n	103	106
LS mean (SE)	1.86 (1.86)	1.67 (1.83)
95% CI of LS mean	(-1.81, 5.53)	(-1.95, 5.29)
P-value within Treatment	0.3197	0.3641
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.19 (-5.36, 4.99)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9424
Hedges' G (SE)		-0.01 (0.14)
Hedges' 95% CI		(-0.28, 0.26)
Hedges' P-value		0.9422

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	24	26
Mean (SD)	70.83 (35.86)	83.33 (25.39)
Week 8 (MMRM)		
n	24	24
LS mean (SE)	74.56 (6.01)	89.59 (5.93)
95% CI of LS mean	(62.44, 86.68)	(77.64, 101.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	15.02 (-2.30, 32.35)
Absolute Change at Week 8 (MMRM)		
n	24	24
LS mean (SE)	1.58 (4.08)	6.83 (4.05)
95% CI of LS mean	(-6.69, 9.84)	(-1.38, 15.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.26 (-6.66, 17.18)
Week 16 (MMRM)		
n	22	23
LS mean (SE)	75.21 (6.11)	90.79 (5.98)
95% CI of LS mean	(62.84, 87.58)	(78.70, 102.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	15.58 (-2.02, 33.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 16 (MMRM)		
n	22	23
LS mean (SE)	1.95 (6.08)	9.44 (5.91)
95% CI of LS mean	(-10.33, 14.23)	(-2.49, 21.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.50 (-9.79, 24.78)
Week 24 (MMRM)		
n	22	22
LS mean (SE)	73.26 (6.43)	91.21 (6.31)
95% CI of LS mean	(60.27, 86.25)	(78.46, 103.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	17.95 (-0.52, 36.43)
Absolute Change at Week 24 (MMRM)		
n	22	22
LS mean (SE)	0.48 (4.54)	9.68 (4.47)
95% CI of LS mean	(-8.70, 9.66)	(0.65, 18.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.20 (-3.89, 22.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52		
n	22	20
Mean (SD)	78.79 (28.26)	91.67 (18.34)
Absolute Change at Week 52		
n	22	20
Mean (SD)	7.58 (25.05)	6.67 (25.59)
Week 52 (MMRM)		
n	22	20
LS mean (SE)	78.20 (5.40)	92.35 (5.48)
95% CI of LS mean	(67.25, 89.15)	(81.27, 103.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.15 (-1.75, 30.06)
Absolute Change at Week 52 (MMRM)		
n	22	20
LS mean (SE)	4.95 (5.26)	11.30 (5.34)
95% CI of LS mean	(-5.66, 15.57)	(0.54, 22.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.35 (-8.95, 21.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change through Week 52 (MMRM)		
n	22	24
LS mean (SE)	2.46 (4.66)	10.14 (4.56)
95% CI of LS mean	(-6.94, 11.86)	(0.95, 19.33)
P-value within Treatment	0.6001	0.0314
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.68 (-5.68, 21.04)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2527
Hedges' G (SE)		0.34 (0.29)
Hedges' 95% CI		(-0.25, 0.93)
Hedges' P-value		0.2487

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	242	240
Mean (SD)	90.22 (21.91)	84.44 (27.25)
Week 8 (MMRM)		
n	238	236
LS mean (SE)	88.59 (1.69)	84.33 (1.70)
95% CI of LS mean	(85.27, 91.91)	(80.99, 87.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.26 (-8.98, 0.46)
Absolute Change at Week 8 (MMRM)		
n	234	233
LS mean (SE)	-2.13 (1.34)	-0.14 (1.34)
95% CI of LS mean	(-4.77, 0.50)	(-2.78, 2.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.99 (-1.74, 5.72)
Week 16 (MMRM)		
n	235	232
LS mean (SE)	87.52 (1.75)	85.16 (1.77)
95% CI of LS mean	(84.07, 90.96)	(81.68, 88.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.36 (-7.26, 2.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 16 (MMRM)		
n	231	229
LS mean (SE)	-3.22 (1.43)	0.69 (1.43)
95% CI of LS mean	(-6.02, -0.41)	(-2.13, 3.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.90 (-0.07, 7.88)
Week 24 (MMRM)		
n	235	229
LS mean (SE)	87.45 (1.77)	84.59 (1.79)
95% CI of LS mean	(83.97, 90.93)	(81.07, 88.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.86 (-7.82, 2.10)
Absolute Change at Week 24 (MMRM)		
n	231	227
LS mean (SE)	-3.14 (1.36)	0.22 (1.37)
95% CI of LS mean	(-5.82, -0.46)	(-2.48, 2.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.35 (-0.45, 7.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52		
n	244	230
Mean (SD)	87.84 (26.06)	83.62 (28.68)
Absolute Change at Week 52		
n	235	227
Mean (SD)	-2.70 (22.16)	-0.73 (21.83)
Week 52 (MMRM)		
n	237	224
LS mean (SE)	87.55 (1.76)	83.38 (1.80)
95% CI of LS mean	(84.09, 91.01)	(79.85, 86.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.17 (-9.12, 0.77)
Absolute Change at Week 52 (MMRM)		
n	228	221
LS mean (SE)	-3.16 (1.48)	-1.00 (1.49)
95% CI of LS mean	(-6.05, -0.26)	(-3.93, 1.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.16 (-1.97, 6.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change through Week 52 (MMRM)		
n	234	230
LS mean (SE)	-3.17 (1.16)	-0.03 (1.17)
95% CI of LS mean	(-5.45, -0.89)	(-2.33, 2.27)
P-value within Treatment	0.0066	0.9791
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.14 (-0.10, 6.38)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0577
Hedges' G (SE)		0.18 (0.09)
Hedges' 95% CI		(-0.01, 0.36)
Hedges' P-value		0.0578

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	76	70
Mean (SD)	89.91 (24.36)	85.24 (26.40)
Week 8 (MMRM)		
n	77	68
LS mean (SE)	89.19 (3.01)	85.92 (3.21)
95% CI of LS mean	(83.24, 95.13)	(79.57, 92.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.26 (-11.98, 5.46)
Absolute Change at Week 8 (MMRM)		
n	75	67
LS mean (SE)	-0.97 (1.97)	0.59 (2.08)
95% CI of LS mean	(-4.87, 2.92)	(-3.53, 4.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.56 (-4.12, 7.25)
Week 16 (MMRM)		
n	75	66
LS mean (SE)	85.85 (3.04)	87.96 (3.25)
95% CI of LS mean	(79.84, 91.86)	(81.52, 94.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.11 (-6.71, 10.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 16 (MMRM)		
n	73	65
LS mean (SE)	-4.40 (1.89)	2.51 (2.00)
95% CI of LS mean	(-8.13, -0.67)	(-1.46, 6.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.91 (1.45, 12.36)
Week 24 (MMRM)		
n	77	62
LS mean (SE)	87.44 (2.90)	86.24 (3.15)
95% CI of LS mean	(81.71, 93.18)	(80.01, 92.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.20 (-9.69, 7.29)
Absolute Change at Week 24 (MMRM)		
n	75	62
LS mean (SE)	-2.75 (1.69)	0.95 (1.84)
95% CI of LS mean	(-6.08, 0.59)	(-2.69, 4.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.70 (-1.25, 8.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52		
n	77	65
Mean (SD)	87.45 (24.80)	85.64 (28.24)
Absolute Change at Week 52		
n	74	64
Mean (SD)	-3.15 (22.19)	0.52 (15.13)
Week 52 (MMRM)		
n	76	62
LS mean (SE)	86.74 (3.00)	85.75 (3.25)
95% CI of LS mean	(80.82, 92.67)	(79.33, 92.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.99 (-9.75, 7.77)
Absolute Change at Week 52 (MMRM)		
n	73	61
LS mean (SE)	-3.53 (2.20)	0.44 (2.39)
95% CI of LS mean	(-7.88, 0.83)	(-4.28, 5.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.97 (-2.46, 10.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change through Week 52 (MMRM)		
n	75	65
LS mean (SE)	-3.56 (1.55)	1.30 (1.66)
95% CI of LS mean	(-6.62, -0.49)	(-1.99, 4.59)
P-value within Treatment	0.0232	0.4358
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.86 (0.35, 9.37)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0350
Hedges' G (SE)		0.36 (0.17)
Hedges' 95% CI		(0.02, 0.70)
Hedges' P-value		0.0358

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	185	194
Mean (SD)	88.29 (23.33)	83.85 (27.40)
Week 8 (MMRM)		
n	185	192
LS mean (SE)	86.57 (1.96)	84.44 (1.93)
95% CI of LS mean	(82.71, 90.42)	(80.65, 88.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.13 (-7.54, 3.28)
Absolute Change at Week 8 (MMRM)		
n	183	190
LS mean (SE)	-1.88 (1.62)	0.32 (1.59)
95% CI of LS mean	(-5.08, 1.31)	(-2.80, 3.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.21 (-2.27, 6.68)
Week 16 (MMRM)		
n	182	189
LS mean (SE)	86.66 (2.04)	84.89 (2.01)
95% CI of LS mean	(82.65, 90.67)	(80.95, 88.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.77 (-7.40, 3.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 16 (MMRM)		
n	180	187
LS mean (SE)	-1.80 (1.83)	0.81 (1.79)
95% CI of LS mean	(-5.39, 1.79)	(-2.71, 4.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.61 (-2.42, 7.64)
Week 24 (MMRM)		
n	180	189
LS mean (SE)	85.73 (2.10)	84.77 (2.06)
95% CI of LS mean	(81.60, 89.87)	(80.71, 88.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.96 (-6.76, 4.84)
Absolute Change at Week 24 (MMRM)		
n	178	187
LS mean (SE)	-2.53 (1.72)	0.83 (1.67)
95% CI of LS mean	(-5.91, 0.84)	(-2.46, 4.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.37 (-1.35, 8.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52		
n	185	183
Mean (SD)	87.39 (26.41)	83.61 (28.14)
Absolute Change at Week 52		
n	179	181
Mean (SD)	-1.30 (23.00)	-0.37 (24.34)
Week 52 (MMRM)		
n	183	182
LS mean (SE)	86.70 (2.02)	83.60 (2.01)
95% CI of LS mean	(82.73, 90.67)	(79.65, 87.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.11 (-8.71, 2.50)
Absolute Change at Week 52 (MMRM)		
n	177	180
LS mean (SE)	-1.69 (1.79)	-0.35 (1.77)
95% CI of LS mean	(-5.22, 1.83)	(-3.83, 3.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.34 (-3.61, 6.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change through Week 52 (MMRM)		
n	181	189
LS mean (SE)	-2.01 (1.48)	0.43 (1.45)
95% CI of LS mean	(-4.91, 0.90)	(-2.41, 3.28)
P-value within Treatment	0.1749	0.7661
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.44 (-1.63, 6.51)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2394
Hedges' G (SE)		0.12 (0.10)
Hedges' 95% CI		(-0.08, 0.33)
Hedges' P-value		0.2395

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	130	141
Mean (SD)	84.62 (27.27)	80.38 (29.83)
Week 8 (MMRM)		
n	127	139
LS mean (SE)	84.48 (2.61)	78.69 (2.50)
95% CI of LS mean	(79.34, 89.61)	(73.75, 83.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.79 (-12.96, 1.38)
Absolute Change at Week 8 (MMRM)		
n	124	137
LS mean (SE)	-1.54 (2.11)	-1.04 (2.01)
95% CI of LS mean	(-5.70, 2.62)	(-5.00, 2.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-5.27, 6.27)
Week 16 (MMRM)		
n	122	135
LS mean (SE)	86.09 (2.52)	81.30 (2.42)
95% CI of LS mean	(81.12, 91.05)	(76.53, 86.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.79 (-11.72, 2.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 16 (MMRM)		
n	119	133
LS mean (SE)	0.17 (2.02)	1.59 (1.91)
95% CI of LS mean	(-3.80, 4.14)	(-2.18, 5.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.42 (-4.08, 6.92)
Week 24 (MMRM)		
n	124	134
LS mean (SE)	82.73 (2.70)	80.89 (2.60)
95% CI of LS mean	(77.41, 88.05)	(75.76, 86.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.84 (-9.27, 5.59)
Absolute Change at Week 24 (MMRM)		
n	121	132
LS mean (SE)	-3.02 (2.04)	1.30 (1.95)
95% CI of LS mean	(-7.04, 0.99)	(-2.53, 5.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.32 (-1.25, 9.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52		
n	132	137
Mean (SD)	84.60 (28.06)	78.83 (31.28)
Absolute Change at Week 52		
n	126	135
Mean (SD)	-0.53 (23.85)	-1.73 (22.79)
Week 52 (MMRM)		
n	126	133
LS mean (SE)	84.40 (2.64)	78.53 (2.56)
95% CI of LS mean	(79.21, 89.59)	(73.49, 83.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.87 (-13.15, 1.41)
Absolute Change at Week 52 (MMRM)		
n	120	131
LS mean (SE)	-1.42 (2.12)	-1.15 (2.03)
95% CI of LS mean	(-5.60, 2.76)	(-5.14, 2.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.27 (-5.53, 6.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change through Week 52 (MMRM)		
n	122	134
LS mean (SE)	-1.42 (1.72)	0.58 (1.64)
95% CI of LS mean	(-4.82, 1.97)	(-2.65, 3.82)
P-value within Treatment	0.4092	0.7241
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.00 (-2.72, 6.73)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4038
Hedges' G (SE)		0.11 (0.12)
Hedges' 95% CI		(-0.14, 0.35)
Hedges' P-value		0.4008

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	136	125
Mean (SD)	92.16 (19.97)	88.80 (22.78)
Week 8 (MMRM)		
n	135	121
LS mean (SE)	90.13 (1.95)	91.70 (2.06)
95% CI of LS mean	(86.28, 93.98)	(87.64, 95.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.57 (-4.06, 7.20)
Absolute Change at Week 8 (MMRM)		
n	134	120
LS mean (SE)	-1.76 (1.53)	2.04 (1.62)
95% CI of LS mean	(-4.78, 1.27)	(-1.14, 5.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.80 (-0.62, 8.21)
Week 16 (MMRM)		
n	135	120
LS mean (SE)	86.92 (2.26)	90.56 (2.39)
95% CI of LS mean	(82.47, 91.37)	(85.87, 95.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.64 (-2.86, 10.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 16 (MMRM)		
n	134	119
LS mean (SE)	-4.99 (1.99)	1.07 (2.10)
95% CI of LS mean	(-8.90, -1.08)	(-3.07, 5.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.05 (0.34, 11.77)
Week 24 (MMRM)		
n	133	117
LS mean (SE)	89.67 (2.11)	89.89 (2.24)
95% CI of LS mean	(85.50, 93.83)	(85.48, 94.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.23 (-5.87, 6.33)
Absolute Change at Week 24 (MMRM)		
n	132	117
LS mean (SE)	-2.25 (1.71)	0.48 (1.81)
95% CI of LS mean	(-5.62, 1.12)	(-3.08, 4.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.73 (-2.19, 7.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52		
n	134	113
Mean (SD)	89.55 (24.33)	90.86 (21.93)
Absolute Change at Week 52		
n	131	112
Mean (SD)	-3.05 (21.26)	1.79 (21.38)
Week 52 (MMRM)		
n	133	111
LS mean (SE)	89.18 (2.03)	90.55 (2.18)
95% CI of LS mean	(85.18, 93.17)	(86.25, 94.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.37 (-4.52, 7.27)
Absolute Change at Week 52 (MMRM)		
n	130	110
LS mean (SE)	-2.88 (1.92)	1.12 (2.06)
95% CI of LS mean	(-6.67, 0.91)	(-2.94, 5.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.00 (-1.58, 9.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change through Week 52 (MMRM)		
n	134	120
LS mean (SE)	-3.37 (1.53)	0.89 (1.62)
95% CI of LS mean	(-6.40, -0.35)	(-2.30, 4.09)
P-value within Treatment	0.0289	0.5836
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.26 (-0.16, 8.69)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0589
Hedges' G (SE)		0.24 (0.13)
Hedges' 95% CI		(-0.01, 0.49)
Hedges' P-value		0.0583

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	99	108
Mean (SD)	89.56 (22.16)	84.26 (28.99)
Week 8 (MMRM)		
n	96	109
LS mean (SE)	89.81 (2.67)	84.95 (2.50)
95% CI of LS mean	(84.54, 95.08)	(80.02, 89.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.86 (-12.08, 2.35)
Absolute Change at Week 8 (MMRM)		
n	95	106
LS mean (SE)	0.76 (1.96)	-0.16 (1.85)
95% CI of LS mean	(-3.11, 4.63)	(-3.81, 3.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.92 (-6.25, 4.42)
Week 16 (MMRM)		
n	94	105
LS mean (SE)	89.07 (2.72)	86.07 (2.56)
95% CI of LS mean	(83.70, 94.44)	(81.03, 91.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.00 (-10.38, 4.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 16 (MMRM)		
n	93	102
LS mean (SE)	0.02 (2.07)	0.91 (1.97)
95% CI of LS mean	(-4.07, 4.10)	(-2.97, 4.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.89 (-4.75, 6.53)
Week 24 (MMRM)		
n	95	105
LS mean (SE)	89.54 (2.71)	84.59 (2.55)
95% CI of LS mean	(84.20, 94.88)	(79.57, 89.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.95 (-12.29, 2.39)
Absolute Change at Week 24 (MMRM)		
n	94	103
LS mean (SE)	0.87 (1.92)	-0.44 (1.82)
95% CI of LS mean	(-2.91, 4.66)	(-4.04, 3.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.31 (-6.55, 3.92)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52		
n	98	101
Mean (SD)	92.52 (20.60)	82.84 (31.13)
Absolute Change at Week 52		
n	97	98
Mean (SD)	3.44 (20.12)	-2.72 (23.29)
Week 52 (MMRM)		
n	94	101
LS mean (SE)	91.83 (2.71)	83.39 (2.56)
95% CI of LS mean	(86.49, 97.17)	(78.33, 88.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.44 (-15.80, -1.08)
Absolute Change at Week 52 (MMRM)		
n	93	98
LS mean (SE)	3.12 (2.26)	-1.70 (2.18)
95% CI of LS mean	(-1.34, 7.59)	(-6.00, 2.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.83 (-11.03, 1.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change through Week 52 (MMRM)		
n	95	104
LS mean (SE)	1.34 (1.76)	-0.41 (1.68)
95% CI of LS mean	(-2.14, 4.82)	(-3.72, 2.90)
P-value within Treatment	0.4496	0.8061
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.75 (-6.56, 3.06)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4742
Hedges' G (SE)		-0.10 (0.14)
Hedges' 95% CI		(-0.38, 0.18)
Hedges' P-value		0.4736

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	167	158
Mean (SD)	87.82 (25.18)	84.39 (25.70)
Week 8 (MMRM)		
n	166	151
LS mean (SE)	85.61 (2.04)	85.13 (2.15)
95% CI of LS mean	(81.59, 89.62)	(80.90, 89.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-6.31, 5.37)
Absolute Change at Week 8 (MMRM)		
n	163	151
LS mean (SE)	-3.05 (1.67)	0.85 (1.74)
95% CI of LS mean	(-6.34, 0.24)	(-2.56, 4.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.91 (-0.84, 8.65)
Week 16 (MMRM)		
n	163	150
LS mean (SE)	84.57 (2.13)	85.83 (2.24)
95% CI of LS mean	(80.39, 88.76)	(81.43, 90.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.26 (-4.82, 7.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	160	150
LS mean (SE)	-4.13 (1.86)	1.63 (1.92)
95% CI of LS mean	(-7.79, -0.47)	(-2.16, 5.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.76 (0.49, 11.03)
Week 24 (MMRM)		
n	162	146
LS mean (SE)	84.00 (2.19)	85.98 (2.31)
95% CI of LS mean	(79.71, 88.30)	(81.44, 90.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.98 (-4.28, 8.24)
Absolute Change at Week 24 (MMRM)		
n	159	146
LS mean (SE)	-4.70 (1.76)	1.92 (1.83)
95% CI of LS mean	(-8.15, -1.24)	(-1.68, 5.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.62 (1.62, 11.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52		
n	168	149
Mean (SD)	83.93 (28.72)	85.23 (25.81)
Absolute Change at Week 52		
n	160	149
Mean (SD)	-5.00 (23.41)	1.57 (21.34)
Week 52 (MMRM)		
n	165	143
LS mean (SE)	83.46 (2.10)	85.09 (2.24)
95% CI of LS mean	(79.32, 87.59)	(80.67, 89.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.63 (-4.43, 7.69)
Absolute Change at Week 52 (MMRM)		
n	157	143
LS mean (SE)	-5.48 (1.81)	1.11 (1.89)
95% CI of LS mean	(-9.04, -1.91)	(-2.62, 4.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.58 (1.42, 11.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	161	150
LS mean (SE)	-4.77 (1.47)	1.55 (1.52)
95% CI of LS mean	(-7.66, -1.88)	(-1.45, 4.55)
P-value within Treatment	0.0013	0.3096
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.32 (2.15, 10.49)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0031
Hedges' G (SE)		0.34 (0.11)
Hedges' 95% CI		(0.11, 0.56)
Hedges' P-value		0.0032

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.1055
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.1474
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.8496
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.3931
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.7479
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.0846
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.4636
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.3388
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.4644
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.3907
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	87.04 (21.56)	77.78 (22.22)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	88.45 (8.50)	85.40 (9.31)
95% CI of LS mean	(70.27, 106.63)	(65.81, 104.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.05 (-31.32, 25.22)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	1.52 (11.47)	7.42 (12.06)
95% CI of LS mean	(-24.84, 27.88)	(-21.90, 36.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.90 (-35.90, 47.69)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	86.90 (8.30)	89.10 (9.31)
95% CI of LS mean	(69.04, 104.75)	(69.52, 108.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.20 (-25.66, 30.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	-7.20 (10.83)	18.53 (12.06)
95% CI of LS mean	(-32.24, 17.83)	(-10.79, 47.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	25.73 (-14.78, 66.24)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	85.02 (7.73)	80.20 (8.16)
95% CI of LS mean	(67.94, 102.10)	(62.48, 97.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.82 (-31.22, 21.58)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	-6.87 (9.09)	16.57 (10.71)
95% CI of LS mean	(-30.85, 17.11)	(-11.87, 45.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	23.44 (-17.03, 63.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	92.06 (16.62)	87.04 (12.99)
Absolute Change at Week 52		
n	5	3
Mean (SD)	2.22 (9.30)	18.52 (16.97)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	92.43 (7.73)	85.35 (7.73)
95% CI of LS mean	(75.35, 109.50)	(68.27, 102.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.08 (-33.06, 18.91)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	1.46 (9.09)	20.27 (10.71)
95% CI of LS mean	(-22.52, 25.45)	(-8.16, 48.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	18.81 (-21.66, 59.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	-4.20 (7.92)	18.46 (9.42)
95% CI of LS mean	(-31.22, 22.82)	(-13.59, 50.50)
P-value within Treatment	0.6364	0.1556
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	22.66 (-23.81, 69.12)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1991
Hedges' G (SE)		1.19 (0.72)
Hedges' 95% CI		(-0.65, 3.03)
Hedges' P-value		0.1581

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	72.22 (25.09)	88.89 (16.67)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	62.75 (8.82)	92.74 (7.15)
95% CI of LS mean	(43.52, 81.98)	(77.13, 108.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	29.99 (4.86, 55.11)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	-7.44 (8.04)	2.49 (6.52)
95% CI of LS mean	(-24.99, 10.10)	(-11.75, 16.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.94 (-12.98, 32.86)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	76.90 (5.38)	99.03 (4.13)
95% CI of LS mean	(65.11, 88.69)	(89.92, 108.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	22.14 (6.50, 37.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	5.55 (8.87)	8.95 (7.25)
95% CI of LS mean	(-13.80, 24.91)	(-6.87, 24.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.39 (-21.83, 28.62)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	73.86 (4.85)	96.50 (3.93)
95% CI of LS mean	(63.20, 84.52)	(87.90, 105.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	22.64 (8.23, 37.06)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	3.67 (7.23)	6.36 (5.95)
95% CI of LS mean	(-12.18, 19.51)	(-6.63, 19.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.69 (-18.18, 23.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-cg-52wks-sub-103.sas Creation: 13JAN2025 12:20

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	91.67 (16.67)	95.24 (8.74)
Absolute Change at Week 52		
n	4	7
Mean (SD)	11.11 (30.09)	-1.59 (4.20)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	77.30 (8.41)	98.77 (6.67)
95% CI of LS mean	(57.93, 96.66)	(83.23, 114.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	21.48 (-3.60, 46.55)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	5.89 (10.41)	6.39 (8.14)
95% CI of LS mean	(-17.64, 29.42)	(-12.10, 24.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-29.61, 30.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	5.04 (7.99)	7.23 (6.46)
95% CI of LS mean	(-12.77, 22.85)	(-7.16, 21.63)
P-value within Treatment	0.5428	0.2892
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.20 (-21.02, 25.42)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8372
Hedges' G (SE)		0.11 (0.50)
Hedges' 95% CI		(-0.97, 1.18)
Hedges' P-value		0.8339

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	83.33 (15.32)	92.59 (12.83)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	83.02 (7.06)	89.91 (7.64)
95% CI of LS mean	(67.86, 98.18)	(73.78, 106.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.89 (-16.62, 30.40)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	4.35 (6.22)	4.31 (6.32)
95% CI of LS mean	(-9.43, 18.13)	(-10.04, 18.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-20.76, 20.68)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	80.44 (6.92)	82.50 (7.64)
95% CI of LS mean	(65.50, 95.38)	(66.37, 98.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.06 (-21.17, 25.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	-1.61 (5.81)	-12.36 (6.32)
95% CI of LS mean	(-14.43, 11.22)	(-26.71, 2.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-10.75 (-30.19, 8.69)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	87.14 (6.52)	89.52 (6.82)
95% CI of LS mean	(72.74, 101.55)	(74.68, 104.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-19.85, 24.61)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	6.62 (4.59)	-5.12 (5.39)
95% CI of LS mean	(-4.22, 17.45)	(-17.91, 7.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-11.74 (-29.71, 6.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	84.13 (15.53)	88.89 (9.94)
Absolute Change at Week 52		
n	5	3
Mean (SD)	0.00 (0.00)	3.70 (6.42)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	83.44 (6.52)	86.93 (6.52)
95% CI of LS mean	(69.03, 97.85)	(72.52, 101.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.49 (-18.45, 25.44)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	1.06 (4.59)	2.29 (5.39)
95% CI of LS mean	(-9.78, 11.90)	(-10.50, 15.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.23 (-16.74, 19.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	2.02 (3.69)	-5.06 (4.41)
95% CI of LS mean	(-8.94, 12.99)	(-18.15, 8.03)
P-value within Treatment	0.6175	0.3246
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.09 (-25.90, 11.73)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3235
Hedges' G (SE)		-0.80 (0.68)
Hedges' 95% CI		(-2.54, 0.94)
Hedges' P-value		0.2925

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	81.48 (20.69)	86.42 (9.26)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	78.30 (8.54)	82.37 (6.78)
95% CI of LS mean	(59.53, 97.06)	(67.48, 97.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.08 (-21.45, 29.60)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	-0.98 (4.97)	-5.52 (3.97)
95% CI of LS mean	(-11.84, 9.88)	(-14.21, 3.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.54 (-19.11, 10.03)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	73.17 (8.79)	84.07 (6.65)
95% CI of LS mean	(53.96, 92.39)	(69.38, 98.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.90 (-15.00, 36.79)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	-6.95 (6.27)	-4.27 (4.75)
95% CI of LS mean	(-20.69, 6.79)	(-14.87, 6.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.68 (-15.27, 20.64)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	65.33 (9.22)	92.19 (7.53)
95% CI of LS mean	(44.06, 86.61)	(74.91, 109.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	26.86 (-1.91, 55.63)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	-13.94 (6.25)	4.20 (5.28)
95% CI of LS mean	(-28.41, 0.52)	(-7.95, 16.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	18.14 (-1.18, 37.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	80.56 (13.98)	80.95 (15.33)
Absolute Change at Week 52		
n	4	7
Mean (SD)	-11.11 (12.83)	-3.17 (8.40)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	64.15 (10.37)	80.74 (7.92)
95% CI of LS mean	(37.59, 90.71)	(59.46, 102.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	16.59 (-18.35, 51.53)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	-16.17 (8.06)	-7.42 (6.18)
95% CI of LS mean	(-35.13, 2.79)	(-22.43, 7.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.75 (-15.67, 33.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	-12.35 (5.25)	-2.49 (4.13)
95% CI of LS mean	(-24.90, 0.19)	(-12.62, 7.63)
P-value within Treatment	0.0526	0.5679
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.86 (-6.78, 26.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2029
Hedges' G (SE)		0.74 (0.51)
Hedges' 95% CI		(-0.37, 1.85)
Hedges' P-value		0.1744

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	97.22 (6.80)	88.89 (9.62)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	88.53 (5.57)	89.79 (6.27)
95% CI of LS mean	(76.96, 100.10)	(76.84, 102.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.26 (-16.83, 19.35)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	0.46 (3.98)	1.69 (4.33)
95% CI of LS mean	(-9.08, 10.01)	(-9.37, 12.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.22 (-14.46, 16.91)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	97.47 (5.39)	100.90 (6.27)
95% CI of LS mean	(86.25, 108.69)	(87.95, 113.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.43 (-14.19, 21.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	0.27 (3.83)	10.02 (4.33)
95% CI of LS mean	(-9.05, 9.60)	(-1.04, 21.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.75 (-5.82, 25.31)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	94.53 (4.83)	96.74 (5.21)
95% CI of LS mean	(84.31, 104.75)	(85.82, 107.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.21 (-13.66, 18.08)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	0.39 (3.40)	10.59 (4.01)
95% CI of LS mean	(-8.98, 9.76)	(-0.52, 21.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.20 (-5.61, 26.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	100.00 (0.00)	100.00 (0.00)
Absolute Change at Week 52		
n	5	3
Mean (SD)	0.00 (0.00)	11.11 (9.62)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	100.08 (4.83)	99.92 (4.83)
95% CI of LS mean	(89.86, 110.31)	(89.69, 110.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-15.56, 15.22)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	0.39 (3.40)	10.59 (4.01)
95% CI of LS mean	(-8.98, 9.76)	(-0.52, 21.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.20 (-5.61, 26.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	0.35 (3.12)	10.40 (3.71)
95% CI of LS mean	(-9.73, 10.43)	(-1.53, 22.34)
P-value within Treatment	0.9178	0.0691
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.05 (-7.05, 27.15)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1539
Hedges' G (SE)		1.34 (0.74)
Hedges' 95% CI		(-0.55, 3.23)
Hedges' P-value		0.1283

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	91.67 (20.41)	92.59 (16.90)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	82.94 (7.55)	98.41 (6.03)
95% CI of LS mean	(66.41, 99.47)	(85.18, 111.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	15.47 (-6.70, 37.65)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	-8.88 (4.22)	5.92 (3.42)
95% CI of LS mean	(-18.01, 0.26)	(-1.49, 13.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.79 (2.84, 26.75)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	88.66 (7.13)	94.50 (5.75)
95% CI of LS mean	(73.02, 104.30)	(81.88, 107.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.84 (-15.30, 26.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	-3.75 (2.78)	2.12 (2.25)
95% CI of LS mean	(-9.77, 2.26)	(-2.76, 7.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.87 (-2.25, 14.00)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	88.49 (6.53)	96.66 (5.23)
95% CI of LS mean	(74.00, 102.99)	(85.09, 108.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.17 (-11.61, 27.95)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	-3.32 (3.94)	4.11 (3.41)
95% CI of LS mean	(-11.87, 5.23)	(-3.25, 11.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.43 (-4.06, 18.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	100.00 (0.00)	92.86 (13.11)
Absolute Change at Week 52		
n	4	7
Mean (SD)	0.00 (0.00)	-7.14 (13.11)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	84.87 (11.18)	89.04 (8.58)
95% CI of LS mean	(57.96, 111.78)	(67.80, 110.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.17 (-30.22, 38.57)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	2.00 (8.77)	-8.22 (5.78)
95% CI of LS mean	(-18.97, 22.96)	(-22.52, 6.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-10.21 (-35.70, 15.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	-1.69 (3.61)	-0.66 (2.54)
95% CI of LS mean	(-22.08, 18.69)	(-16.29, 14.96)
P-value within Treatment	0.6964	0.8255
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.03 (-24.44, 26.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8476
Hedges' G (SE)		0.12 (0.50)
Hedges' 95% CI		(-0.95, 1.19)
Hedges' P-value		0.8138

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	86.67 (13.98)	80.00 (20.00)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	83.19 (7.26)	83.81 (7.65)
95% CI of LS mean	(67.26, 99.13)	(67.32, 100.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.62 (-23.96, 25.19)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	-0.32 (8.12)	8.25 (9.25)
95% CI of LS mean	(-22.16, 21.52)	(-18.02, 34.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.57 (-28.55, 45.68)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	84.74 (7.17)	88.25 (7.65)
95% CI of LS mean	(68.93, 100.56)	(71.76, 104.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.51 (-20.91, 27.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	12.01 (7.98)	8.25 (9.25)
95% CI of LS mean	(-9.88, 33.90)	(-18.02, 34.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.76 (-41.15, 33.63)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	81.13 (6.92)	86.81 (7.11)
95% CI of LS mean	(65.60, 96.66)	(71.04, 102.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.68 (-18.20, 29.56)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	-0.03 (7.57)	11.16 (8.95)
95% CI of LS mean	(-22.69, 22.62)	(-15.70, 38.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.19 (-27.00, 49.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	88.57 (12.00)	81.11 (14.86)
Absolute Change at Week 52		
n	5	3
Mean (SD)	1.33 (14.45)	4.44 (10.18)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	83.35 (6.92)	85.54 (6.92)
95% CI of LS mean	(67.82, 98.88)	(70.01, 101.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.19 (-21.54, 25.91)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	-0.03 (7.57)	8.93 (8.95)
95% CI of LS mean	(-22.69, 22.62)	(-17.92, 35.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.97 (-29.22, 47.15)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	3.98 (7.32)	9.45 (8.67)
95% CI of LS mean	(-19.53, 27.49)	(-18.37, 37.27)
P-value within Treatment	0.6249	0.3568
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.47 (-34.13, 45.06)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6864
Hedges' G (SE)		0.31 (0.65)
Hedges' 95% CI		(-1.36, 1.98)
Hedges' P-value		0.6517

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	77.78 (18.70)	79.26 (19.56)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	84.29 (5.83)	91.22 (4.70)
95% CI of LS mean	(71.34, 97.23)	(80.75, 101.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.93 (-10.12, 23.98)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	6.95 (6.89)	11.66 (5.52)
95% CI of LS mean	(-8.12, 22.03)	(-0.43, 23.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.71 (-15.43, 24.85)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	75.72 (7.98)	85.95 (6.56)
95% CI of LS mean	(57.90, 93.54)	(71.33, 100.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.22 (-13.03, 33.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	-0.49 (6.75)	5.55 (5.44)
95% CI of LS mean	(-15.47, 14.50)	(-6.53, 17.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.04 (-14.04, 26.11)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	78.73 (7.48)	88.12 (6.16)
95% CI of LS mean	(62.17, 95.29)	(74.55, 101.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.39 (-12.32, 31.11)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	1.40 (7.60)	8.16 (6.20)
95% CI of LS mean	(-15.25, 18.04)	(-5.39, 21.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.76 (-15.40, 28.92)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	78.33 (11.39)	81.90 (10.69)
Absolute Change at Week 52		
n	4	7
Mean (SD)	-1.67 (19.91)	-4.76 (13.72)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	78.30 (5.53)	78.94 (4.05)
95% CI of LS mean	(65.90, 90.71)	(69.73, 88.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.64 (-15.41, 16.70)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	-0.91 (7.74)	-4.69 (5.62)
95% CI of LS mean	(-17.92, 16.11)	(-17.25, 7.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.78 (-25.79, 18.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	0.00 (6.11)	3.01 (4.82)
95% CI of LS mean	(-14.17, 14.18)	(-8.17, 14.18)
P-value within Treatment	0.9998	0.5505
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.00 (-16.11, 22.12)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7247
Hedges' G (SE)		0.19 (0.50)
Hedges' 95% CI		(-0.88, 1.27)
Hedges' P-value		0.7041

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	87.04 (10.92)	88.89 (19.25)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	78.85 (9.02)	70.50 (9.90)
95% CI of LS mean	(59.62, 98.08)	(49.73, 91.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.34 (-38.26, 21.57)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	-14.70 (9.41)	-4.35 (9.94)
95% CI of LS mean	(-36.48, 7.09)	(-28.81, 20.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.34 (-24.47, 45.15)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	81.52 (8.80)	81.61 (9.90)
95% CI of LS mean	(62.65, 100.39)	(60.84, 102.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.09 (-29.37, 29.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	-0.37 (8.91)	-9.91 (9.94)
95% CI of LS mean	(-21.16, 20.41)	(-34.36, 14.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.54 (-43.45, 24.37)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	80.43 (8.18)	81.12 (8.64)
95% CI of LS mean	(62.43, 98.43)	(62.41, 99.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.69 (-27.14, 28.53)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	-8.30 (7.54)	-3.74 (8.89)
95% CI of LS mean	(-28.51, 11.90)	(-27.71, 20.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.56 (-29.58, 38.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	87.30 (10.00)	79.63 (16.36)
Absolute Change at Week 52		
n	5	3
Mean (SD)	-2.22 (14.49)	-11.11 (11.11)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	85.99 (8.18)	82.53 (8.18)
95% CI of LS mean	(67.99, 103.98)	(64.53, 100.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.45 (-30.82, 23.92)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	-2.75 (7.54)	-7.45 (8.89)
95% CI of LS mean	(-22.95, 17.46)	(-31.41, 16.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.70 (-38.84, 29.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	-3.81 (6.63)	-7.03 (7.89)
95% CI of LS mean	(-26.64, 19.02)	(-34.09, 20.03)
P-value within Treatment	0.6110	0.4460
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.22 (-42.43, 35.98)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7918
Hedges' G (SE)		-0.20 (0.65)
Hedges' 95% CI		(-1.86, 1.46)
Hedges' P-value		0.7666

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	72.22 (13.61)	71.60 (24.91)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	69.80 (7.01)	84.33 (5.66)
95% CI of LS mean	(54.59, 85.00)	(72.05, 96.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.54 (-5.50, 34.58)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	-0.29 (8.86)	11.30 (7.11)
95% CI of LS mean	(-19.62, 19.04)	(-4.23, 26.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.59 (-14.13, 37.31)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	69.70 (8.27)	70.64 (6.06)
95% CI of LS mean	(51.57, 87.84)	(57.22, 84.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (-22.17, 24.04)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	-1.87 (8.96)	-0.22 (6.64)
95% CI of LS mean	(-21.50, 17.77)	(-14.96, 14.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.64 (-24.06, 27.35)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	77.20 (6.29)	83.58 (5.32)
95% CI of LS mean	(63.37, 91.03)	(71.93, 95.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.38 (-12.23, 25.00)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	7.12 (9.85)	11.81 (8.19)
95% CI of LS mean	(-14.39, 28.63)	(-6.01, 29.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.69 (-24.00, 33.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	86.11 (13.98)	82.54 (19.09)
Absolute Change at Week 52		
n	4	7
Mean (SD)	8.33 (10.64)	1.59 (23.51)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	80.35 (9.39)	82.06 (7.07)
95% CI of LS mean	(59.91, 100.78)	(66.53, 97.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.71 (-24.27, 27.69)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	10.23 (12.12)	11.34 (9.45)
95% CI of LS mean	(-17.08, 37.54)	(-10.20, 32.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.12 (-34.15, 36.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	5.16 (8.70)	7.64 (6.85)
95% CI of LS mean	(-13.85, 24.17)	(-7.39, 22.67)
P-value within Treatment	0.5645	0.2876
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.48 (-22.74, 27.71)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8336
Hedges' G (SE)		0.11 (0.50)
Hedges' 95% CI		(-0.96, 1.18)
Hedges' P-value		0.8248

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	88.89 (11.69)	97.22 (4.81)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	91.57 (4.40)	99.43 (4.81)
95% CI of LS mean	(82.25, 100.89)	(89.37, 109.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.86 (-6.64, 22.35)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	4.88 (2.97)	-1.01 (3.28)
95% CI of LS mean	(-2.46, 12.21)	(-9.65, 7.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.89 (-18.11, 6.34)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	91.19 (4.29)	99.43 (4.81)
95% CI of LS mean	(82.04, 100.34)	(89.37, 109.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.23 (-6.04, 22.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	5.56 (2.88)	-3.09 (3.28)
95% CI of LS mean	(-1.68, 12.80)	(-11.73, 5.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.65 (-20.88, 3.57)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	84.04 (4.00)	102.11 (4.22)
95% CI of LS mean	(75.33, 92.75)	(93.05, 111.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	18.07 (4.61, 31.53)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	3.11 (2.61)	1.41 (3.08)
95% CI of LS mean	(-4.30, 10.51)	(-7.37, 10.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.69 (-14.20, 10.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	91.07 (10.04)	99.31 (1.70)
Absolute Change at Week 52		
n	5	3
Mean (SD)	1.67 (9.13)	2.78 (4.81)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	90.29 (4.00)	102.07 (4.00)
95% CI of LS mean	(81.58, 99.00)	(93.36, 110.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.79 (-1.45, 25.02)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	6.23 (2.61)	1.41 (3.08)
95% CI of LS mean	(-1.17, 13.64)	(-7.37, 10.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.82 (-17.33, 7.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	4.97 (2.44)	-0.09 (2.89)
95% CI of LS mean	(-2.94, 12.88)	(-9.45, 9.27)
P-value within Treatment	0.1374	0.9776
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.05 (-18.44, 8.33)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3066
Hedges' G (SE)		-0.86 (0.68)
Hedges' 95% CI		(-2.62, 0.89)
Hedges' P-value		0.2618

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	83.33 (17.28)	81.48 (23.02)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	88.79 (5.19)	90.34 (4.14)
95% CI of LS mean	(77.36, 100.23)	(81.22, 99.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.55 (-13.87, 16.97)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	6.34 (6.05)	8.27 (4.93)
95% CI of LS mean	(-6.74, 19.42)	(-2.37, 18.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.93 (-14.99, 18.85)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	84.13 (5.94)	92.21 (4.76)
95% CI of LS mean	(71.11, 97.15)	(81.77, 102.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.08 (-9.27, 25.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	1.41 (6.32)	10.08 (5.12)
95% CI of LS mean	(-12.24, 15.05)	(-0.98, 21.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.68 (-8.94, 26.30)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	80.26 (5.67)	90.28 (4.75)
95% CI of LS mean	(67.68, 92.84)	(79.79, 100.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.02 (-7.03, 27.07)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	-2.19 (8.95)	8.32 (7.41)
95% CI of LS mean	(-21.53, 17.15)	(-7.63, 24.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.51 (-14.60, 35.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\t-qs-mmrm-abs-cfqr-nonrd-cg-52wks-sub-103.sas Creation: 13JAN2025 12:20

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	98.96 (2.08)	88.10 (15.11)
Absolute Change at Week 52		
n	4	7
Mean (SD)	10.42 (15.77)	-1.19 (7.87)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	93.98 (5.28)	87.47 (4.17)
95% CI of LS mean	(82.30, 105.66)	(78.22, 96.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.51 (-22.19, 9.17)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	10.27 (5.39)	3.41 (4.38)
95% CI of LS mean	(-1.41, 21.95)	(-6.06, 12.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.85 (-21.96, 8.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	3.16 (6.35)	7.27 (5.19)
95% CI of LS mean	(-10.57, 16.89)	(-3.93, 18.48)
P-value within Treatment	0.6272	0.1843
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.11 (-13.67, 21.89)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6258
Hedges' G (SE)		0.25 (0.50)
Hedges' 95% CI		(-0.83, 1.32)
Hedges' P-value		0.6260

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	84.72 (11.08)	86.11 (12.73)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	81.29 (6.97)	80.13 (7.63)
95% CI of LS mean	(66.49, 96.09)	(64.15, 96.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.16 (-24.18, 21.86)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	3.72 (7.01)	4.94 (7.57)
95% CI of LS mean	(-12.85, 20.29)	(-14.08, 23.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.22 (-25.77, 28.21)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	81.57 (6.80)	88.46 (7.63)
95% CI of LS mean	(67.04, 96.09)	(72.48, 104.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.90 (-15.77, 29.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	-8.83 (6.72)	4.94 (7.57)
95% CI of LS mean	(-24.93, 7.27)	(-14.08, 23.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	13.77 (-12.88, 40.42)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	81.42 (6.33)	83.67 (6.68)
95% CI of LS mean	(67.59, 95.26)	(69.28, 98.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.25 (-19.15, 23.64)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	-7.16 (5.89)	3.99 (6.95)
95% CI of LS mean	(-23.13, 8.81)	(-14.95, 22.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.14 (-15.80, 38.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	76.98 (14.05)	79.17 (12.64)
Absolute Change at Week 52		
n	5	3
Mean (SD)	-13.89 (14.57)	-2.78 (4.81)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	72.63 (6.33)	82.46 (6.33)
95% CI of LS mean	(58.79, 86.46)	(68.63, 96.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.84 (-11.19, 30.86)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	-18.27 (5.89)	1.21 (6.95)
95% CI of LS mean	(-34.24, -2.30)	(-17.73, 20.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	19.48 (-7.47, 46.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	-11.42 (5.36)	3.38 (6.36)
95% CI of LS mean	(-28.64, 5.80)	(-17.01, 23.76)
P-value within Treatment	0.1244	0.6327
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.80 (-14.44, 44.04)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2003
Hedges' G (SE)		1.15 (0.71)
Hedges' 95% CI		(-0.68, 2.98)
Hedges' P-value		0.1677

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	73.61 (31.81)	80.56 (16.14)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	68.43 (5.45)	86.79 (4.44)
95% CI of LS mean	(56.50, 80.35)	(77.08, 96.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	18.37 (2.91, 33.82)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	-1.71 (8.43)	3.92 (6.83)
95% CI of LS mean	(-20.65, 17.23)	(-11.44, 19.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.62 (-19.18, 30.43)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	69.31 (7.28)	83.74 (6.08)
95% CI of LS mean	(53.33, 85.29)	(70.46, 97.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.43 (-6.44, 35.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	-3.84 (6.23)	0.88 (4.95)
95% CI of LS mean	(-17.58, 9.89)	(-9.98, 11.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.72 (-13.57, 23.01)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	69.81 (9.87)	89.22 (8.12)
95% CI of LS mean	(48.44, 91.19)	(71.67, 106.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	19.40 (-8.30, 47.11)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	-0.32 (8.52)	5.52 (7.22)
95% CI of LS mean	(-19.61, 18.97)	(-10.59, 21.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.84 (-19.71, 31.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	79.17 (25.00)	79.76 (17.25)
Absolute Change at Week 52		
n	4	7
Mean (SD)	-2.08 (23.94)	-5.95 (13.36)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	81.75 (10.39)	80.42 (8.34)
95% CI of LS mean	(59.14, 104.35)	(62.23, 98.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.32 (-30.41, 27.76)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	-3.96 (10.83)	-7.26 (7.79)
95% CI of LS mean	(-29.13, 21.20)	(-25.46, 10.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.30 (-35.01, 28.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	-2.71 (7.03)	-0.29 (5.44)
95% CI of LS mean	(-21.67, 16.26)	(-14.70, 14.13)
P-value within Treatment	0.7183	0.9602
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.42 (-22.37, 27.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8043
Hedges' G (SE)		0.14 (0.50)
Hedges' 95% CI		(-0.94, 1.21)
Hedges' P-value		0.7874

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	66.67 (31.43)	62.96 (12.83)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	60.86 (11.08)	82.82 (12.08)
95% CI of LS mean	(37.29, 84.44)	(57.47, 108.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	21.96 (-14.67, 58.59)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	6.12 (13.35)	16.92 (13.74)
95% CI of LS mean	(-23.83, 36.08)	(-15.15, 48.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.79 (-35.25, 56.83)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	55.30 (10.83)	82.82 (12.08)
95% CI of LS mean	(32.14, 78.47)	(57.47, 108.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	27.52 (-8.59, 63.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	-5.51 (12.48)	16.92 (13.74)
95% CI of LS mean	(-33.50, 22.48)	(-15.15, 48.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	22.42 (-21.29, 66.13)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	56.84 (10.13)	81.55 (10.65)
95% CI of LS mean	(34.71, 78.98)	(58.60, 104.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	24.71 (-9.49, 58.91)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	-5.67 (10.11)	18.68 (11.89)
95% CI of LS mean	(-30.76, 19.41)	(-11.00, 48.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	24.35 (-17.64, 66.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	66.67 (25.66)	68.52 (10.92)
Absolute Change at Week 52		
n	5	3
Mean (SD)	-4.44 (25.58)	11.11 (22.22)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	60.55 (10.13)	74.64 (10.13)
95% CI of LS mean	(38.41, 82.68)	(52.50, 96.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.09 (-19.57, 47.75)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	-2.90 (10.11)	11.27 (11.89)
95% CI of LS mean	(-27.98, 22.19)	(-18.41, 40.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.16 (-27.83, 56.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	-4.69 (8.44)	15.62 (10.07)
95% CI of LS mean	(-32.03, 22.64)	(-16.93, 48.17)
P-value within Treatment	0.6183	0.2210
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	20.31 (-26.88, 67.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2501
Hedges' G (SE)		1.00 (0.70)
Hedges' 95% CI		(-0.79, 2.79)
Hedges' P-value		0.2106

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	55.56 (32.20)	66.67 (22.22)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	73.69 (12.70)	65.69 (10.25)
95% CI of LS mean	(43.38, 104.00)	(41.15, 90.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.00 (-47.78, 31.79)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	13.80 (6.27)	1.91 (5.02)
95% CI of LS mean	(0.09, 27.52)	(-9.09, 12.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-11.90 (-30.23, 6.44)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	64.55 (9.21)	62.46 (7.11)
95% CI of LS mean	(42.79, 86.31)	(45.43, 79.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.09 (-31.16, 26.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	-0.65 (8.91)	-0.88 (7.40)
95% CI of LS mean	(-20.97, 19.66)	(-17.95, 16.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-27.08, 26.64)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	58.87 (12.04)	69.68 (9.98)
95% CI of LS mean	(31.35, 86.39)	(46.97, 92.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.81 (-25.75, 47.37)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	-1.01 (7.78)	6.00 (6.50)
95% CI of LS mean	(-18.88, 16.86)	(-8.86, 20.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.01 (-16.75, 30.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	61.11 (19.25)	69.84 (18.94)
Absolute Change at Week 52		
n	4	7
Mean (SD)	-2.78 (24.64)	0.00 (12.83)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	55.84 (11.84)	66.28 (9.12)
95% CI of LS mean	(27.36, 84.31)	(43.88, 88.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.44 (-26.74, 47.62)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	-4.11 (8.54)	3.30 (6.70)
95% CI of LS mean	(-22.82, 14.60)	(-11.52, 18.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.41 (-16.91, 31.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	-1.93 (7.18)	2.81 (5.87)
95% CI of LS mean	(-18.74, 14.89)	(-10.98, 16.59)
P-value within Treatment	0.7959	0.6465
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.73 (-17.49, 26.96)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6344
Hedges' G (SE)		0.25 (0.50)
Hedges' 95% CI		(-0.82, 1.33)
Hedges' P-value		0.6199

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	70.28 (22.96)	75.56 (15.40)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	73.41 (9.77)	72.03 (10.64)
95% CI of LS mean	(52.64, 94.19)	(49.71, 94.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.39 (-33.66, 30.88)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	18.29 (11.68)	1.65 (13.43)
95% CI of LS mean	(-13.89, 50.47)	(-37.04, 40.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-16.64 (-71.33, 38.05)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	74.72 (9.56)	74.25 (10.64)
95% CI of LS mean	(54.30, 95.14)	(51.94, 96.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-32.29, 31.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	27.37 (11.53)	-8.35 (13.43)
95% CI of LS mean	(-4.95, 59.68)	(-47.04, 30.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-35.72 (-90.77, 19.33)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	71.60 (8.94)	67.21 (9.40)
95% CI of LS mean	(52.09, 91.12)	(46.98, 87.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.39 (-34.54, 25.76)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	20.11 (11.08)	-9.58 (13.11)
95% CI of LS mean	(-13.13, 53.34)	(-48.98, 29.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-29.69 (-85.64, 26.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	79.05 (18.23)	77.78 (10.89)
Absolute Change at Week 52		
n	5	3
Mean (SD)	9.00 (20.67)	6.67 (11.55)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	76.05 (8.94)	79.51 (8.94)
95% CI of LS mean	(56.53, 95.56)	(59.99, 99.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.46 (-26.21, 33.14)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	16.77 (11.08)	-0.70 (13.11)
95% CI of LS mean	(-16.46, 50.01)	(-40.09, 38.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-17.47 (-73.42, 38.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	21.42 (10.81)	-6.21 (12.81)
95% CI of LS mean	(-12.70, 55.53)	(-46.58, 34.16)
P-value within Treatment	0.1406	0.6605
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-27.63 (-84.99, 29.74)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2237
Hedges' G (SE)		-1.06 (0.70)
Hedges' 95% CI		(-2.87, 0.74)
Hedges' P-value		0.1906

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	75.56 (13.11)	68.15 (18.19)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	76.21 (8.27)	75.12 (6.61)
95% CI of LS mean	(57.34, 95.08)	(59.96, 90.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.09 (-26.22, 24.04)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	0.49 (0.00)	7.08 (0.00)
95% CI of LS mean	(-, -)	(-, -)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.60 (-, -)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	83.37 (6.46)	67.91 (4.61)
95% CI of LS mean	(68.85, 97.89)	(57.60, 78.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-15.46 (-35.26, 4.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	8.32 (0.00)	0.70 (0.00)
95% CI of LS mean	(-, -)	(-, -)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.62 (-, -)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	69.54 (9.38)	71.77 (7.70)
95% CI of LS mean	(48.71, 90.37)	(54.73, 88.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.23 (-25.53, 29.99)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	-6.18 (0.00)	4.35 (0.00)
95% CI of LS mean	(-, -)	(-, -)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.53 (-, -)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	85.00 (3.33)	72.38 (19.41)
Absolute Change at Week 52		
n	4	7
Mean (SD)	5.00 (13.74)	0.00 (12.17)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	82.89 (9.09)	70.90 (7.11)
95% CI of LS mean	(60.60, 105.18)	(52.68, 89.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-11.99 (-40.95, 16.97)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	15.78 (0.00)	12.29 (0.00)
95% CI of LS mean	(-, -)	(-, -)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.49 (-, -)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	5.97 (0.00)	5.78 (0.00)
95% CI of LS mean	(-, -)	(-, -)
P-value within Treatment	<0.0001	<0.0001
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.20 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-
Hedges' 95% CI		-
Hedges' P-value		-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	88.89 (17.21)	66.67 (33.33)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	86.71 (14.77)	50.60 (16.22)
95% CI of LS mean	(54.95, 118.46)	(16.39, 84.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-36.11 (-85.50, 13.29)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	-8.89 (15.79)	-7.18 (14.66)
95% CI of LS mean	(-43.78, 26.00)	(-39.68, 25.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.71 (-47.39, 50.82)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	89.27 (14.41)	61.71 (16.22)
95% CI of LS mean	(58.08, 120.46)	(27.50, 95.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-27.56 (-76.26, 21.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	-7.74 (13.76)	9.49 (14.66)
95% CI of LS mean	(-37.73, 22.26)	(-23.01, 41.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	17.23 (-25.09, 59.54)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	88.42 (13.40)	79.12 (14.16)
95% CI of LS mean	(58.50, 118.33)	(48.11, 110.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.30 (-55.56, 36.97)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	-10.72 (9.75)	14.29 (11.39)
95% CI of LS mean	(-32.37, 10.93)	(-11.09, 39.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	25.01 (-10.04, 60.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	95.24 (12.60)	66.67 (42.16)
Absolute Change at Week 52		
n	5	3
Mean (SD)	0.00 (23.57)	22.22 (19.25)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	99.53 (13.40)	61.58 (13.40)
95% CI of LS mean	(69.61, 129.45)	(31.67, 91.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-37.95 (-83.51, 7.62)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	-2.38 (9.75)	14.29 (11.39)
95% CI of LS mean	(-24.04, 19.27)	(-11.09, 39.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	16.67 (-18.38, 51.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	-6.95 (6.33)	12.69 (7.66)
95% CI of LS mean	(-27.99, 14.10)	(-14.32, 39.70)
P-value within Treatment	0.3582	0.2119
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	19.63 (-21.17, 60.44)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1819
Hedges' G (SE)		1.28 (0.73)
Hedges' 95% CI		(-0.59, 3.15)
Hedges' P-value		0.1390

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	83.33 (27.89)	85.19 (24.22)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	73.56 (9.23)	88.00 (7.44)
95% CI of LS mean	(53.96, 93.16)	(72.21, 103.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.44 (-11.53, 40.41)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	-10.23 (13.34)	3.11 (10.74)
95% CI of LS mean	(-39.19, 18.74)	(-20.19, 26.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	13.34 (-25.14, 51.82)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	79.04 (9.63)	87.31 (7.64)
95% CI of LS mean	(58.81, 99.27)	(71.19, 103.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.27 (-18.40, 34.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	-4.34 (13.62)	2.56 (10.88)
95% CI of LS mean	(-33.68, 25.01)	(-20.94, 26.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.89 (-32.00, 45.79)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	79.11 (9.23)	91.47 (7.64)
95% CI of LS mean	(59.51, 98.72)	(75.36, 107.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	12.36 (-13.80, 38.52)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	-4.67 (13.34)	6.72 (10.88)
95% CI of LS mean	(-33.64, 24.30)	(-16.77, 30.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.39 (-27.20, 49.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	83.33 (33.33)	100.00 (0.00)
Absolute Change at Week 52		
n	4	7
Mean (SD)	-16.67 (33.33)	14.29 (26.23)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	79.94 (10.13)	98.94 (7.86)
95% CI of LS mean	(58.87, 101.01)	(82.48, 115.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	18.99 (-8.49, 46.48)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	-4.61 (13.98)	13.93 (11.03)
95% CI of LS mean	(-34.47, 25.24)	(-9.77, 37.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	18.55 (-20.85, 57.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	-4.54 (12.79)	7.74 (10.26)
95% CI of LS mean	(-32.86, 23.78)	(-15.00, 30.48)
P-value within Treatment	0.7297	0.4675
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	12.28 (-25.40, 49.95)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4861
Hedges' G (SE)		0.37 (0.50)
Hedges' 95% CI		(-0.71, 1.45)
Hedges' P-value		0.4698

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.0543
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.0409
Sex (Male vs. Female) [1]	0.8477
Region (North America vs. Rest of the World) [1]	0.7737

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.12.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.9848
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.6004
Sex (Male vs. Female) [1]	0.8520
Region (North America vs. Rest of the World) [1]	0.5898

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.12.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.7787
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.9212
Sex (Male vs. Female) [1]	0.8364
Region (North America vs. Rest of the World) [1]	0.8641

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.12.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.4637
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.3046
Sex (Male vs. Female) [1]	0.7828
Region (North America vs. Rest of the World) [1]	0.3462

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	6
Mean (SD)	79.63 (20.39)	73.15 (15.08)
Week 52		
n	5	6
Mean (SD)	75.56 (30.07)	84.26 (18.40)
Absolute Change at Week 52		
n	5	6
Mean (SD)	-10.00 (25.58)	11.11 (13.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52 (MMRM)		
n	4	6
LS mean (SE)	-5.50 (10.88)	5.52 (8.33)
95% CI of LS mean	(-33.47, 22.48)	(-15.91, 26.94)
P-value within Treatment	0.6349	0.5372
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.01 (-29.22, 51.25)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5130
Hedges' G (SE)		0.48 (0.59)
Hedges' 95% CI		(-0.89, 1.84)
Hedges' P-value		0.4457

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 34
Baseline		
n	29	31
Mean (SD)	81.61 (17.00)	81.00 (18.07)
Week 52		
n	30	33
Mean (SD)	89.44 (11.88)	81.99 (19.84)
Absolute Change at Week 52		
n	28	30
Mean (SD)	8.13 (19.63)	1.48 (20.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 52 (MMRM)		
n	27	30
LS mean (SE)	9.08 (4.02)	0.53 (3.81)
95% CI of LS mean	(1.00, 17.17)	(-7.13, 8.18)
P-value within Treatment	0.0284	0.8902
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.55 (-19.88, 2.78)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1357
Hedges' G (SE)		-0.40 (0.26)
Hedges' 95% CI		(-0.93, 0.13)
Hedges' P-value		0.1323

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment,and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Age at screening ≥18 years

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment,and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
Baseline		
n	8	10
Mean (SD)	90.28 (13.85)	71.11 (22.95)
Week 52		
n	8	10
Mean (SD)	96.53 (6.60)	88.89 (17.57)
Absolute Change at Week 52		
n	8	9
Mean (SD)	6.25 (11.67)	16.05 (20.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 52 (MMRM)		
n	8	9
LS mean (SE)	1.82 (6.97)	19.99 (6.43)
95% CI of LS mean	(-13.72, 17.35)	(5.66, 34.32)
P-value within Treatment	0.7998	0.0111
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	18.17 (-6.58, 42.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1329
Hedges' G (SE)		0.88 (0.49)
Hedges' 95% CI		(-0.15, 1.92)
Hedges' P-value		0.0884

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 30
Baseline		
n	25	28
Mean (SD)	79.11 (17.88)	82.14 (14.84)
Week 52		
n	25	29
Mean (SD)	85.11 (17.03)	80.08 (19.78)
Absolute Change at Week 52		
n	23	27
Mean (SD)	4.83 (24.69)	-1.23 (17.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 30
Absolute Change at Week 52 (MMRM)		
n	23	27
LS mean (SE)	5.02 (4.48)	-1.40 (4.13)
95% CI of LS mean	(-4.02, 14.06)	(-9.72, 6.93)
P-value within Treatment	0.2690	0.7369
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.42 (-18.87, 6.04)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3046
Hedges' G (SE)		-0.29 (0.28)
Hedges' 95% CI		(-0.86, 0.27)
Hedges' P-value		0.3003

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Male

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 15
Baseline		
n	20	13
Mean (SD)	80.56 (16.67)	80.34 (17.22)
Week 52		
n	20	15
Mean (SD)	90.00 (11.20)	79.26 (23.33)
Absolute Change at Week 52		
n	18	13
Mean (SD)	8.33 (16.42)	4.70 (15.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Male

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	16	13
LS mean (SE)	7.22 (4.29)	6.08 (4.79)
95% CI of LS mean	(-1.65, 16.08)	(-3.81, 15.96)
P-value within Treatment	0.1059	0.2168
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.14 (-14.75, 12.46)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8640
Hedges' G (SE)		-0.06 (0.36)
Hedges' 95% CI		(-0.81, 0.68)
Hedges' P-value		0.8605

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Female

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 26
Baseline		
n	15	25
Mean (SD)	82.22 (18.69)	78.67 (18.26)
Week 52		
n	15	24
Mean (SD)	84.07 (20.45)	84.26 (16.76)
Absolute Change at Week 52		
n	15	23
Mean (SD)	1.85 (26.03)	2.17 (22.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Female

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	15	23
LS mean (SE)	2.45 (6.55)	1.78 (5.27)
95% CI of LS mean	(-10.90, 15.81)	(-8.96, 12.52)
P-value within Treatment	0.7107	0.7372
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.67 (-17.97, 16.64)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9377
Hedges' G (SE)		-0.03 (0.32)
Hedges' 95% CI		(-0.68, 0.63)
Hedges' P-value		0.9370

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = North America

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 15
Baseline		
n	9	13
Mean (SD)	85.19 (13.32)	76.07 (19.82)
Week 52		
n	9	13
Mean (SD)	91.36 (11.49)	84.19 (10.84)
Absolute Change at Week 52		
n	8	11
Mean (SD)	6.94 (16.47)	3.03 (12.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = North America

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	8	11
LS mean (SE)	11.24 (5.63)	-0.09 (4.60)
95% CI of LS mean	(-0.83, 23.31)	(-9.97, 9.78)
P-value within Treatment	0.0656	0.9839
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-11.34 (-28.82, 6.15)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1861
Hedges' G (SE)		-0.70 (0.46)
Hedges' 95% CI		(-1.66, 0.27)
Hedges' P-value		0.1465

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = Rest of World

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 26
Baseline		
n	26	25
Mean (SD)	79.91 (18.53)	80.89 (16.67)
Week 52		
n	26	26
Mean (SD)	86.11 (17.09)	81.41 (22.66)
Absolute Change at Week 52		
n	25	25
Mean (SD)	4.89 (22.81)	3.11 (22.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = Rest of World

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	23	25
LS mean (SE)	5.51 (4.94)	2.27 (4.73)
95% CI of LS mean	(-4.46, 15.47)	(-7.28, 11.81)
P-value within Treatment	0.2714	0.6343
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.24 (-17.24, 10.77)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6434
Hedges' G (SE)		-0.13 (0.28)
Hedges' 95% CI		(-0.71, 0.44)
Hedges' P-value		0.6388

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	6
Mean (SD)	100.00 (0.00)	93.75 (9.68)
Week 52		
n	5	6
Mean (SD)	100.00 (0.00)	97.92 (5.10)
Absolute Change at Week 52		
n	5	6
Mean (SD)	0.00 (0.00)	4.17 (7.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52 (MMRM)		
n	4	6
LS mean (SE)	0.39 (4.51)	3.91 (3.46)
95% CI of LS mean	(-11.21, 11.99)	(-4.98, 12.79)
P-value within Treatment	0.9343	0.3096
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.52 (-13.17, 20.20)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6113
Hedges' G (SE)		0.37 (0.59)
Hedges' 95% CI		(-0.99, 1.72)
Hedges' P-value		0.5516

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 34
Baseline		
n	29	31
Mean (SD)	100.00 (0.00)	95.36 (12.81)
Week 52		
n	30	33
Mean (SD)	93.33 (15.91)	96.21 (14.06)
Absolute Change at Week 52		
n	28	30
Mean (SD)	-7.14 (16.38)	-0.42 (13.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 52 (MMRM)		
n	27	30
LS mean (SE)	-6.85 (3.01)	-0.92 (2.85)
95% CI of LS mean	(-12.90, -0.80)	(-6.64, 4.81)
P-value within Treatment	0.0272	0.7491
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.93 (-2.54, 14.41)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1660
Hedges' G (SE)		0.37 (0.26)
Hedges' 95% CI		(-0.15, 0.90)
Hedges' P-value		0.1617

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment,and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Age at screening ≥18 years

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment,and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
Baseline		
n	8	10
Mean (SD)	100.00 (0.00)	91.25 (11.86)
Week 52		
n	8	10
Mean (SD)	92.19 (14.85)	98.75 (3.95)
Absolute Change at Week 52		
n	8	9
Mean (SD)	-7.81 (14.85)	4.86 (8.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 52 (MMRM)		
n	8	9
LS mean (SE)	-4.93 (5.82)	2.30 (5.37)
95% CI of LS mean	(-17.90, 8.04)	(-9.66, 14.26)
P-value within Treatment	0.4168	0.6775
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.23 (-13.44, 27.90)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4537
Hedges' G (SE)		0.42 (0.47)
Hedges' 95% CI		(-0.57, 1.42)
Hedges' P-value		0.3806

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 30
Baseline		
n	25	28
Mean (SD)	100.00 (0.00)	96.65 (12.09)
Week 52		
n	25	29
Mean (SD)	94.50 (15.66)	95.69 (14.95)
Absolute Change at Week 52		
n	23	27
Mean (SD)	-5.98 (16.26)	-1.16 (13.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 30
Absolute Change at Week 52 (MMRM)		
n	23	27
LS mean (SE)	-6.32 (3.27)	-0.87 (3.01)
95% CI of LS mean	(-12.91, 0.27)	(-6.94, 5.20)
P-value within Treatment	0.0598	0.7746
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.45 (-3.63, 14.53)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2326
Hedges' G (SE)		0.34 (0.28)
Hedges' 95% CI		(-0.22, 0.91)
Hedges' P-value		0.2292

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Male

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 15
Baseline		
n	20	13
Mean (SD)	100.00 (0.00)	99.04 (3.47)
Week 52		
n	20	15
Mean (SD)	94.69 (16.38)	100.00 (0.00)
Absolute Change at Week 52		
n	18	13
Mean (SD)	-5.90 (17.21)	0.96 (3.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Male

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	16	13
LS mean (SE)	-7.55 (3.58)	2.08 (3.99)
95% CI of LS mean	(-14.94, -0.16)	(-6.16, 10.32)
P-value within Treatment	0.0455	0.6067
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.63 (-1.71, 20.97)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0923
Hedges' G (SE)		0.65 (0.37)
Hedges' 95% CI		(-0.11, 1.42)
Hedges' P-value		0.0915

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Female

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 26
Baseline		
n	15	25
Mean (SD)	100.00 (0.00)	93.25 (14.42)
Week 52		
n	15	24
Mean (SD)	93.75 (13.15)	94.27 (16.37)
Absolute Change at Week 52		
n	15	23
Mean (SD)	-6.25 (13.15)	0.00 (15.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Female

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	15	23
LS mean (SE)	-5.96 (3.93)	-0.19 (3.16)
95% CI of LS mean	(-13.98, 2.05)	(-6.63, 6.26)
P-value within Treatment	0.1393	0.9531
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.78 (-4.61, 16.16)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2654
Hedges' G (SE)		0.37 (0.33)
Hedges' 95% CI		(-0.29, 1.04)
Hedges' P-value		0.2632

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = North America

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 15
Baseline		
n	9	13
Mean (SD)	100.00 (0.00)	97.60 (8.67)
Week 52		
n	9	13
Mean (SD)	95.83 (12.50)	100.00 (0.00)
Absolute Change at Week 52		
n	8	11
Mean (SD)	-4.69 (13.26)	0.00 (0.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = North America

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	8	11
LS mean (SE)	-2.49 (3.29)	-1.60 (2.69)
95% CI of LS mean	(-9.54, 4.57)	(-7.37, 4.17)
P-value within Treatment	0.4626	0.5613
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.88 (-9.34, 11.11)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8555
Hedges' G (SE)		0.09 (0.44)
Hedges' 95% CI		(-0.84, 1.03)
Hedges' P-value		0.8367

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = Rest of World

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 26
Baseline		
n	26	25
Mean (SD)	100.00 (0.00)	94.00 (13.56)
Week 52		
n	26	26
Mean (SD)	93.75 (15.81)	94.71 (15.78)
Absolute Change at Week 52		
n	25	25
Mean (SD)	-6.50 (16.08)	0.50 (15.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = Rest of World

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	23	25
LS mean (SE)	-6.71 (3.45)	0.18 (3.31)
95% CI of LS mean	(-13.67, 0.25)	(-6.49, 6.84)
P-value within Treatment	0.0582	0.9578
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.89 (-2.89, 16.67)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1626
Hedges' G (SE)		0.41 (0.29)
Hedges' 95% CI		(-0.17, 0.99)
Hedges' P-value		0.1605

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	5
Mean (SD)	71.30 (14.24)	92.22 (12.17)
Week 52		
n	5	6
Mean (SD)	74.44 (18.68)	87.04 (19.14)
Absolute Change at Week 52		
n	5	5
Mean (SD)	0.00 (17.12)	-4.44 (10.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52 (MMRM)		
n	4	5
LS mean (SE)	2.74 (11.25)	-6.64 (9.71)
95% CI of LS mean	(-28.50, 33.98)	(-33.60, 20.33)
P-value within Treatment	0.8194	0.5318
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.38 (-56.69, 37.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6113
Hedges' G (SE)		-0.38 (0.60)
Hedges' 95% CI		(-1.80, 1.05)
Hedges' P-value		0.5505

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 34
Baseline		
n	29	31
Mean (SD)	84.48 (14.88)	82.80 (15.20)
Week 52		
n	30	33
Mean (SD)	87.41 (13.21)	84.68 (11.95)
Absolute Change at Week 52		
n	28	30
Mean (SD)	2.98 (15.60)	0.56 (17.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 52 (MMRM)		
n	27	30
LS mean (SE)	2.87 (3.32)	0.38 (3.15)
95% CI of LS mean	(-3.81, 9.54)	(-5.93, 6.70)
P-value within Treatment	0.3924	0.9034
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.48 (-11.83, 6.87)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5963
Hedges' G (SE)		-0.14 (0.26)
Hedges' 95% CI		(-0.67, 0.38)
Hedges' P-value		0.5900

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment,and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Age at screening ≥18 years

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment,and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
Baseline		
n	8	9
Mean (SD)	88.19 (11.67)	83.33 (20.79)
Week 52		
n	8	10
Mean (SD)	90.97 (12.58)	87.22 (16.15)
Absolute Change at Week 52		
n	8	8
Mean (SD)	2.78 (9.85)	0.00 (12.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 52 (MMRM)		
n	8	8
LS mean (SE)	2.03 (4.21)	0.75 (4.21)
95% CI of LS mean	(-7.49, 11.54)	(-8.76, 10.27)
P-value within Treatment	0.6415	0.8621
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.27 (-17.23, 14.68)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8606
Hedges' G (SE)		-0.10 (0.47)
Hedges' 95% CI		(-1.12, 0.91)
Hedges' P-value		0.8336

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 30
Baseline		
n	25	28
Mean (SD)	80.67 (16.44)	82.94 (14.89)
Week 52		
n	25	29
Mean (SD)	84.00 (14.73)	84.29 (11.98)
Absolute Change at Week 52		
n	23	27
Mean (SD)	2.17 (17.86)	-0.21 (17.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 30
Absolute Change at Week 52 (MMRM)		
n	23	27
LS mean (SE)	1.41 (3.83)	0.44 (3.53)
95% CI of LS mean	(-6.31, 9.13)	(-6.67, 7.55)
P-value within Treatment	0.7144	0.9002
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.97 (-11.60, 9.67)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8556
Hedges' G (SE)		-0.05 (0.28)
Hedges' 95% CI		(-0.61, 0.51)
Hedges' P-value		0.8537

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Male

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 15
Baseline		
n	20	13
Mean (SD)	85.56 (15.02)	88.03 (12.39)
Week 52		
n	20	15
Mean (SD)	88.33 (14.63)	86.67 (12.56)
Absolute Change at Week 52		
n	18	13
Mean (SD)	1.23 (13.00)	-0.43 (20.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Male

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	16	13
LS mean (SE)	0.13 (4.55)	0.27 (5.08)
95% CI of LS mean	(-9.27, 9.52)	(-10.21, 10.75)
P-value within Treatment	0.9778	0.9580
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-14.28, 14.56)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9839
Hedges' G (SE)		0.01 (0.36)
Hedges' 95% CI		(-0.74, 0.75)
Hedges' P-value		0.9835

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Female

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 26
Baseline		
n	15	24
Mean (SD)	77.78 (15.29)	80.32 (17.57)
Week 52		
n	15	24
Mean (SD)	81.85 (14.00)	84.03 (13.44)
Absolute Change at Week 52		
n	15	22
Mean (SD)	4.07 (18.60)	0.00 (13.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Female

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	15	22
LS mean (SE)	3.59 (4.30)	0.33 (3.54)
95% CI of LS mean	(-5.19, 12.37)	(-6.89, 7.55)
P-value within Treatment	0.4103	0.9261
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.26 (-14.74, 8.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5664
Hedges' G (SE)		-0.19 (0.33)
Hedges' 95% CI		(-0.86, 0.47)
Hedges' P-value		0.5626

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = North America

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 15
Baseline		
n	9	13
Mean (SD)	88.27 (14.01)	81.62 (19.95)
Week 52		
n	9	13
Mean (SD)	83.33 (17.79)	85.47 (13.90)
Absolute Change at Week 52		
n	8	11
Mean (SD)	-4.17 (16.99)	-4.04 (21.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = North America

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	8	11
LS mean (SE)	-2.54 (9.08)	-5.22 (7.42)
95% CI of LS mean	(-22.00, 16.93)	(-21.14, 10.69)
P-value within Treatment	0.7838	0.4930
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.69 (-30.88, 25.51)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8411
Hedges' G (SE)		-0.10 (0.44)
Hedges' 95% CI		(-1.04, 0.83)
Hedges' P-value		0.8204

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = Rest of World

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 26
Baseline		
n	26	24
Mean (SD)	80.13 (15.57)	83.80 (14.18)
Week 52		
n	26	26
Mean (SD)	86.32 (13.54)	84.83 (12.82)
Absolute Change at Week 52		
n	25	24
Mean (SD)	4.67 (14.84)	1.62 (13.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = Rest of World

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	23	24
LS mean (SE)	4.27 (3.11)	1.93 (3.04)
95% CI of LS mean	(-2.01, 10.55)	(-4.21, 8.07)
P-value within Treatment	0.1773	0.5300
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.34 (-11.25, 6.56)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5984
Hedges' G (SE)		-0.15 (0.29)
Hedges' 95% CI		(-0.73, 0.42)
Hedges' P-value		0.5938

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	6
Mean (SD)	86.90 (10.51)	87.62 (15.95)
Week 52		
n	5	6
Mean (SD)	72.86 (35.14)	84.52 (18.85)
Absolute Change at Week 52		
n	5	6
Mean (SD)	-14.29 (28.12)	-3.10 (4.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52 (MMRM)		
n	4	6
LS mean (SE)	-3.41 (5.44)	-11.54 (4.17)
95% CI of LS mean	(-17.39, 10.57)	(-22.24, -0.83)
P-value within Treatment	0.5583	0.0394
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.13 (-28.24, 11.98)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3465
Hedges' G (SE)		-0.70 (0.60)
Hedges' 95% CI		(-2.09, 0.69)
Hedges' P-value		0.2787

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 34
Baseline		
n	29	31
Mean (SD)	86.21 (13.22)	86.41 (14.80)
Week 52		
n	30	33
Mean (SD)	92.62 (8.89)	89.39 (11.59)
Absolute Change at Week 52		
n	28	30
Mean (SD)	6.38 (15.59)	2.62 (17.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 52 (MMRM)		
n	27	30
LS mean (SE)	6.61 (3.27)	2.38 (3.10)
95% CI of LS mean	(0.04, 13.18)	(-3.84, 8.61)
P-value within Treatment	0.0487	0.4450
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.22 (-13.43, 4.99)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3613
Hedges' G (SE)		-0.25 (0.26)
Hedges' 95% CI		(-0.77, 0.28)
Hedges' P-value		0.3542

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment,and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Age at screening ≥18 years

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment,and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
Baseline		
n	8	10
Mean (SD)	87.50 (17.39)	81.86 (19.55)
Week 52		
n	8	10
Mean (SD)	94.64 (9.92)	90.00 (16.56)
Absolute Change at Week 52		
n	8	9
Mean (SD)	7.14 (22.26)	7.46 (19.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 52 (MMRM)		
n	8	9
LS mean (SE)	3.23 (7.78)	10.94 (7.18)
95% CI of LS mean	(-14.11, 20.56)	(-5.05, 26.93)
P-value within Treatment	0.6873	0.1583
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.72 (-19.91, 35.34)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5475
Hedges' G (SE)		0.34 (0.46)
Hedges' 95% CI		(-0.65, 1.33)
Hedges' P-value		0.4799

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 30
Baseline		
n	25	28
Mean (SD)	86.57 (11.54)	87.50 (13.13)
Week 52		
n	25	29
Mean (SD)	89.14 (17.87)	88.18 (11.50)
Absolute Change at Week 52		
n	23	27
Mean (SD)	2.17 (18.83)	-0.26 (15.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 30
Absolute Change at Week 52 (MMRM)		
n	23	27
LS mean (SE)	1.52 (3.23)	0.29 (2.97)
95% CI of LS mean	(-4.99, 8.03)	(-5.70, 6.29)
P-value within Treatment	0.6404	0.9217
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.22 (-10.19, 7.74)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7844
Hedges' G (SE)		-0.08 (0.28)
Hedges' 95% CI		(-0.64, 0.48)
Hedges' P-value		0.7815

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Male

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 15
Baseline		
n	20	13
Mean (SD)	85.71 (12.26)	86.26 (16.61)
Week 52		
n	20	15
Mean (SD)	93.21 (9.41)	90.00 (11.71)
Absolute Change at Week 52		
n	18	13
Mean (SD)	7.54 (15.97)	5.49 (14.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Male

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	16	13
LS mean (SE)	6.83 (3.47)	7.53 (3.87)
95% CI of LS mean	(-0.35, 14.00)	(-0.46, 15.53)
P-value within Treatment	0.0612	0.0637
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.71 (-10.30, 11.72)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8954
Hedges' G (SE)		0.05 (0.36)
Hedges' 95% CI		(-0.70, 0.79)
Hedges' P-value		0.8927

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Female

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 26
Baseline		
n	15	25
Mean (SD)	87.14 (13.55)	85.89 (14.46)
Week 52		
n	15	24
Mean (SD)	85.24 (21.84)	87.80 (13.57)
Absolute Change at Week 52		
n	15	23
Mean (SD)	-1.90 (21.51)	-0.50 (17.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Female

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	15	23
LS mean (SE)	-1.57 (4.72)	-0.71 (3.79)
95% CI of LS mean	(-11.20, 8.05)	(-8.45, 7.03)
P-value within Treatment	0.7408	0.8524
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.86 (-11.61, 13.33)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8887
Hedges' G (SE)		0.05 (0.32)
Hedges' 95% CI		(-0.61, 0.71)
Hedges' P-value		0.8874

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = North America

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 15
Baseline		
n	9	13
Mean (SD)	86.51 (16.15)	86.26 (15.28)
Week 52		
n	9	13
Mean (SD)	96.03 (9.52)	87.36 (10.17)
Absolute Change at Week 52		
n	8	11
Mean (SD)	10.71 (21.26)	-3.25 (16.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = North America

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	8	11
LS mean (SE)	10.91 (7.72)	-3.39 (6.31)
95% CI of LS mean	(-5.65, 27.47)	(-16.93, 10.15)
P-value within Treatment	0.1794	0.5997
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-14.30 (-38.28, 9.68)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2217
Hedges' G (SE)		-0.64 (0.46)
Hedges' 95% CI		(-1.60, 0.32)
Hedges' P-value		0.1777

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = Rest of World

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 26
Baseline		
n	26	25
Mean (SD)	86.26 (11.59)	85.89 (15.18)
Week 52		
n	26	26
Mean (SD)	87.64 (17.56)	89.29 (14.03)
Absolute Change at Week 52		
n	25	25
Mean (SD)	0.86 (18.01)	3.83 (16.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = Rest of World

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	23	25
LS mean (SE)	1.69 (3.49)	3.13 (3.34)
95% CI of LS mean	(-5.35, 8.73)	(-3.61, 9.87)
P-value within Treatment	0.6304	0.3544
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.44 (-8.45, 11.33)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7706
Hedges' G (SE)		0.08 (0.28)
Hedges' 95% CI		(-0.49, 0.66)
Hedges' P-value		0.7673

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.2898
Age at screening (<18 years vs. ≥18 years) [2]	0.5505
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.8899
Sex (Male vs. Female) [1]	0.5485
Region (North America vs. Rest of the World) [1]	0.0380

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.13.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Physical Activity

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.4437
Age at screening (<18 years vs. ≥18 years) [2]	0.9537
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.1701
Sex (Male vs. Female) [1]	0.3132
Region (North America vs. Rest of the World) [1]	0.1154

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.13.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Social Activity

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.2463
Age at screening (<18 years vs. ≥18 years) [2]	0.2028
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.6120
Sex (Male vs. Female) [1]	0.5613
Region (North America vs. Rest of the World) [1]	0.9871

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.13.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Emotional

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.4207
Age at screening (<18 years vs. ≥18 years) [2]	0.8536
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.7220
Sex (Male vs. Female) [1]	0.7024
Region (North America vs. Rest of the World) [1]	0.2562

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.13.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52
Full Analysis Set

Domain: Work/School Limitation

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.8439
Age at screening (<18 years vs. ≥18 years) [2]	0.6397
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.8691
Sex (Male vs. Female) [1]	0.3497
Region (North America vs. Rest of the World) [1]	0.0555

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	160	153
Mean (SD)	10.76 (3.58)	9.84 (3.57)
Week 4 (MMRM)		
n	158	146
LS mean (SE)	10.75 (0.28)	10.08 (0.29)
95% CI of LS mean	(10.20, 11.30)	(9.50, 10.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.67 (-1.47, 0.12)
Absolute Change at Week 4 (MMRM)		
n	152	146
LS mean (SE)	0.01 (0.22)	0.11 (0.22)
95% CI of LS mean	(-0.42, 0.44)	(-0.32, 0.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-0.51, 0.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 24 (MMRM)		
n	154	143
LS mean (SE)	10.94 (0.30)	10.17 (0.31)
95% CI of LS mean	(10.34, 11.54)	(9.55, 10.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.77 (-1.63, 0.09)
Absolute Change at Week 24 (MMRM)		
n	148	142
LS mean (SE)	0.19 (0.24)	0.21 (0.24)
95% CI of LS mean	(-0.28, 0.66)	(-0.27, 0.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.02 (-0.65, 0.69)
Week 52		
n	155	140
Mean (SD)	10.60 (3.97)	9.76 (3.38)
Absolute Change at Week 52		
n	149	139
Mean (SD)	-0.23 (3.00)	0.01 (2.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52 (MMRM)		
n	150	139
LS mean (SE)	10.59 (0.30)	9.86 (0.31)
95% CI of LS mean	(10.01, 11.17)	(9.26, 10.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.73 (-1.57, 0.11)
Absolute Change at Week 52 (MMRM)		
n	144	138
LS mean (SE)	-0.21 (0.24)	-0.05 (0.24)
95% CI of LS mean	(-0.67, 0.26)	(-0.52, 0.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-0.51, 0.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change through Week 52 (MMRM)		
n	151	144
LS mean (SE)	-0.01 (0.20)	0.08 (0.20)
95% CI of LS mean	(-0.39, 0.38)	(-0.31, 0.47)
P-value within Treatment	0.9647	0.6833
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.09 (-0.46, 0.64)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7474
Hedges' G (SE)		0.04 (0.12)
Hedges' 95% CI		(-0.19, 0.27)
Hedges' P-value		0.7472

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	113	124
Mean (SD)	9.74 (3.16)	10.29 (3.70)
Week 4 (MMRM)		
n	115	121
LS mean (SE)	9.72 (0.34)	10.07 (0.33)
95% CI of LS mean	(9.05, 10.40)	(9.41, 10.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.34 (-0.60, 1.28)
Absolute Change at Week 4 (MMRM)		
n	109	120
LS mean (SE)	-0.04 (0.25)	-0.21 (0.24)
95% CI of LS mean	(-0.54, 0.45)	(-0.68, 0.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.16 (-0.85, 0.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 24 (MMRM)		
n	112	114
LS mean (SE)	10.00 (0.34)	10.00 (0.34)
95% CI of LS mean	(9.32, 10.68)	(9.34, 10.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-0.95, 0.96)
Absolute Change at Week 24 (MMRM)		
n	106	113
LS mean (SE)	0.32 (0.29)	-0.19 (0.28)
95% CI of LS mean	(-0.24, 0.89)	(-0.73, 0.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.51 (-1.30, 0.28)
Week 52		
n	115	114
Mean (SD)	9.23 (3.31)	9.39 (3.24)
Absolute Change at Week 52		
n	109	113
Mean (SD)	-0.41 (2.97)	-0.81 (2.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52 (MMRM)		
n	114	113
LS mean (SE)	9.23 (0.31)	9.40 (0.30)
95% CI of LS mean	(8.63, 9.84)	(8.80, 10.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-0.69, 1.02)
Absolute Change at Week 52 (MMRM)		
n	108	112
LS mean (SE)	-0.38 (0.28)	-0.82 (0.28)
95% CI of LS mean	(-0.94, 0.18)	(-1.36, -0.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.44 (-1.22, 0.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change through Week 52 (MMRM)		
n	111	118
LS mean (SE)	-0.03 (0.26)	-0.50 (0.25)
95% CI of LS mean	(-0.53, 0.48)	(-0.99, -0.02)
P-value within Treatment	0.9128	0.0433
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-1.18, 0.23)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1846
Hedges' G (SE)		-0.18 (0.13)
Hedges' 95% CI		(-0.44, 0.08)
Hedges' P-value		0.1840

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	33	40
Mean (SD)	9.21 (2.99)	10.05 (3.69)
Week 4 (MMRM)		
n	35	38
LS mean (SE)	8.32 (0.42)	9.21 (0.40)
95% CI of LS mean	(7.48, 9.16)	(8.41, 10.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.89 (-0.27, 2.05)
Absolute Change at Week 4 (MMRM)		
n	31	37
LS mean (SE)	-0.92 (0.35)	-0.74 (0.32)
95% CI of LS mean	(-1.62, -0.21)	(-1.38, -0.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-0.78, 1.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 24 (MMRM)		
n	33	32
LS mean (SE)	8.47 (0.48)	9.38 (0.48)
95% CI of LS mean	(7.51, 9.43)	(8.43, 10.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.91 (-0.45, 2.27)
Absolute Change at Week 24 (MMRM)		
n	29	31
LS mean (SE)	-0.75 (0.53)	-0.32 (0.50)
95% CI of LS mean	(-1.81, 0.31)	(-1.32, 0.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-1.04, 1.89)
Week 52		
n	35	36
Mean (SD)	8.06 (2.39)	8.69 (2.88)
Absolute Change at Week 52		
n	31	35
Mean (SD)	-0.84 (2.62)	-0.94 (3.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52 (MMRM)		
n	33	36
LS mean (SE)	8.10 (0.47)	8.76 (0.45)
95% CI of LS mean	(7.16, 9.04)	(7.86, 9.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.67 (-0.65, 1.98)
Absolute Change at Week 52 (MMRM)		
n	29	35
LS mean (SE)	-0.88 (0.61)	-1.10 (0.55)
95% CI of LS mean	(-2.09, 0.33)	(-2.20, 0.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.21 (-1.85, 1.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change through Week 52 (MMRM)		
n	30	35
LS mean (SE)	-0.82 (0.52)	-0.71 (0.48)
95% CI of LS mean	(-1.85, 0.22)	(-1.66, 0.24)
P-value within Treatment	0.1191	0.1398
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.11 (-1.30, 1.51)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8812
Hedges' G (SE)		0.04 (0.25)
Hedges' 95% CI		(-0.45, 0.53)
Hedges' P-value		0.8809

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	243	242
Mean (SD)	10.47 (3.47)	10.06 (3.62)
Week 4 (MMRM)		
n	238	229
LS mean (SE)	10.64 (0.24)	10.18 (0.25)
95% CI of LS mean	(10.16, 11.11)	(9.70, 10.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.46 (-1.14, 0.22)
Absolute Change at Week 4 (MMRM)		
n	230	229
LS mean (SE)	0.11 (0.18)	0.07 (0.18)
95% CI of LS mean	(-0.24, 0.47)	(-0.28, 0.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-0.54, 0.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 24 (MMRM)		
n	233	225
LS mean (SE)	10.87 (0.25)	10.19 (0.25)
95% CI of LS mean	(10.38, 11.36)	(9.69, 10.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.68 (-1.38, 0.02)
Absolute Change at Week 24 (MMRM)		
n	225	224
LS mean (SE)	0.38 (0.19)	0.08 (0.20)
95% CI of LS mean	(-0.01, 0.76)	(-0.30, 0.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.29 (-0.84, 0.25)
Week 52		
n	238	222
Mean (SD)	10.29 (3.83)	9.72 (3.35)
Absolute Change at Week 52		
n	230	221
Mean (SD)	-0.22 (3.01)	-0.29 (2.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52 (MMRM)		
n	231	216
LS mean (SE)	10.32 (0.24)	9.77 (0.24)
95% CI of LS mean	(9.86, 10.78)	(9.29, 10.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.55 (-1.22, 0.11)
Absolute Change at Week 52 (MMRM)		
n	223	215
LS mean (SE)	-0.20 (0.19)	-0.30 (0.19)
95% CI of LS mean	(-0.57, 0.17)	(-0.68, 0.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-0.64, 0.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change through Week 52 (MMRM)		
n	232	227
LS mean (SE)	0.09 (0.16)	-0.11 (0.16)
95% CI of LS mean	(-0.23, 0.41)	(-0.43, 0.21)
P-value within Treatment	0.5855	0.5001
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.20 (-0.65, 0.26)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3889
Hedges' G (SE)		-0.08 (0.09)
Hedges' 95% CI		(-0.26, 0.10)
Hedges' P-value		0.3885

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	77	71
Mean (SD)	10.99 (4.08)	10.06 (3.74)
Week 4 (MMRM)		
n	77	67
LS mean (SE)	10.76 (0.44)	10.00 (0.48)
95% CI of LS mean	(9.88, 11.63)	(9.05, 10.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.76 (-2.05, 0.53)
Absolute Change at Week 4 (MMRM)		
n	74	66
LS mean (SE)	-0.29 (0.28)	-0.16 (0.30)
95% CI of LS mean	(-0.85, 0.28)	(-0.76, 0.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-0.70, 0.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 24 (MMRM)		
n	76	60
LS mean (SE)	11.59 (0.47)	10.13 (0.52)
95% CI of LS mean	(10.65, 12.53)	(9.09, 11.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.46 (-2.86, -0.06)
Absolute Change at Week 24 (MMRM)		
n	73	59
LS mean (SE)	0.58 (0.37)	0.15 (0.41)
95% CI of LS mean	(-0.15, 1.31)	(-0.66, 0.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.43 (-1.52, 0.66)
Week 52		
n	78	63
Mean (SD)	10.38 (4.11)	9.13 (2.87)
Absolute Change at Week 52		
n	75	62
Mean (SD)	-0.41 (2.64)	-0.63 (2.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52 (MMRM)		
n	77	60
LS mean (SE)	10.48 (0.42)	9.32 (0.47)
95% CI of LS mean	(9.65, 11.31)	(8.40, 10.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.16 (-2.40, 0.09)
Absolute Change at Week 52 (MMRM)		
n	74	59
LS mean (SE)	-0.38 (0.30)	-0.68 (0.34)
95% CI of LS mean	(-0.98, 0.22)	(-1.35, -0.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-1.20, 0.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change through Week 52 (MMRM)		
n	75	62
LS mean (SE)	0.10 (0.28)	-0.27 (0.31)
95% CI of LS mean	(-0.46, 0.66)	(-0.88, 0.35)
P-value within Treatment	0.7184	0.3972
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.37 (-1.21, 0.47)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3861
Hedges' G (SE)		-0.15 (0.17)
Hedges' 95% CI		(-0.49, 0.19)
Hedges' P-value		0.3852

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	192	209
Mean (SD)	10.06 (3.04)	10.06 (3.60)
Week 4 (MMRM)		
n	196	200
LS mean (SE)	10.15 (0.25)	10.09 (0.24)
95% CI of LS mean	(9.66, 10.63)	(9.61, 10.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-0.74, 0.63)
Absolute Change at Week 4 (MMRM)		
n	187	200
LS mean (SE)	0.07 (0.20)	0.03 (0.19)
95% CI of LS mean	(-0.32, 0.47)	(-0.35, 0.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-0.59, 0.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 24 (MMRM)		
n	190	197
LS mean (SE)	10.14 (0.26)	10.08 (0.25)
95% CI of LS mean	(9.63, 10.64)	(9.59, 10.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-0.76, 0.65)
Absolute Change at Week 24 (MMRM)		
n	181	196
LS mean (SE)	0.09 (0.21)	0.02 (0.20)
95% CI of LS mean	(-0.33, 0.50)	(-0.38, 0.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-0.65, 0.50)
Week 52		
n	189	193
Mean (SD)	9.87 (3.56)	9.71 (3.40)
Absolute Change at Week 52		
n	180	192
Mean (SD)	-0.23 (3.13)	-0.31 (2.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52 (MMRM)		
n	187	192
LS mean (SE)	9.85 (0.25)	9.75 (0.25)
95% CI of LS mean	(9.36, 10.34)	(9.27, 10.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-0.79, 0.59)
Absolute Change at Week 52 (MMRM)		
n	178	191
LS mean (SE)	-0.27 (0.22)	-0.29 (0.22)
95% CI of LS mean	(-0.71, 0.18)	(-0.72, 0.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-0.64, 0.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change through Week 52 (MMRM)		
n	187	200
LS mean (SE)	-0.09 (0.19)	-0.14 (0.18)
95% CI of LS mean	(-0.46, 0.28)	(-0.49, 0.22)
P-value within Treatment	0.6335	0.4428
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-0.56, 0.46)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8497
Hedges' G (SE)		-0.02 (0.10)
Hedges' 95% CI		(-0.22, 0.18)
Hedges' P-value		0.8496

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	137	148
Mean (SD)	9.93 (3.37)	9.43 (3.32)
Week 4 (MMRM)		
n	132	140
LS mean (SE)	9.79 (0.29)	9.50 (0.28)
95% CI of LS mean	(9.22, 10.36)	(8.95, 10.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.29 (-1.09, 0.51)
Absolute Change at Week 4 (MMRM)		
n	126	139
LS mean (SE)	-0.15 (0.21)	0.01 (0.20)
95% CI of LS mean	(-0.57, 0.27)	(-0.39, 0.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-0.43, 0.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 24 (MMRM)		
n	130	138
LS mean (SE)	10.06 (0.30)	9.32 (0.29)
95% CI of LS mean	(9.48, 10.64)	(8.76, 9.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.74 (-1.55, 0.08)
Absolute Change at Week 24 (MMRM)		
n	124	137
LS mean (SE)	0.16 (0.25)	-0.17 (0.24)
95% CI of LS mean	(-0.34, 0.66)	(-0.64, 0.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-1.02, 0.36)
Week 52		
n	137	140
Mean (SD)	9.42 (3.52)	9.09 (3.25)
Absolute Change at Week 52		
n	131	139
Mean (SD)	-0.49 (2.85)	-0.38 (2.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52 (MMRM)		
n	129	136
LS mean (SE)	9.44 (0.29)	9.07 (0.28)
95% CI of LS mean	(8.86, 10.01)	(8.51, 9.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.37 (-1.17, 0.44)
Absolute Change at Week 52 (MMRM)		
n	123	135
LS mean (SE)	-0.49 (0.25)	-0.43 (0.24)
95% CI of LS mean	(-0.98, 0.01)	(-0.90, 0.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-0.63, 0.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change through Week 52 (MMRM)		
n	127	139
LS mean (SE)	-0.16 (0.22)	-0.30 (0.21)
95% CI of LS mean	(-0.60, 0.27)	(-0.72, 0.12)
P-value within Treatment	0.4611	0.1567
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-0.74, 0.47)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6575
Hedges' G (SE)		-0.05 (0.12)
Hedges' 95% CI		(-0.30, 0.19)
Hedges' P-value		0.6559

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	139	134
Mean (SD)	10.69 (3.47)	10.75 (3.83)
Week 4 (MMRM)		
n	141	127
LS mean (SE)	10.78 (0.32)	10.73 (0.34)
95% CI of LS mean	(10.15, 11.42)	(10.06, 11.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-0.98, 0.86)
Absolute Change at Week 4 (MMRM)		
n	135	127
LS mean (SE)	0.13 (0.25)	-0.09 (0.26)
95% CI of LS mean	(-0.36, 0.62)	(-0.60, 0.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-0.93, 0.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 24 (MMRM)		
n	136	119
LS mean (SE)	10.97 (0.34)	10.99 (0.36)
95% CI of LS mean	(10.30, 11.63)	(10.29, 11.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.03 (-0.95, 1.01)
Absolute Change at Week 24 (MMRM)		
n	130	118
LS mean (SE)	0.34 (0.27)	0.25 (0.28)
95% CI of LS mean	(-0.19, 0.87)	(-0.30, 0.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.85, 0.67)
Week 52		
n	136	118
Mean (SD)	10.60 (3.89)	10.15 (3.28)
Absolute Change at Week 52		
n	130	117
Mean (SD)	-0.10 (3.08)	-0.38 (3.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52 (MMRM)		
n	135	116
LS mean (SE)	10.53 (0.31)	10.31 (0.33)
95% CI of LS mean	(9.92, 11.14)	(9.66, 10.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-1.12, 0.68)
Absolute Change at Week 52 (MMRM)		
n	129	115
LS mean (SE)	-0.08 (0.26)	-0.39 (0.28)
95% CI of LS mean	(-0.60, 0.44)	(-0.94, 0.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-1.07, 0.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change through Week 52 (MMRM)		
n	135	123
LS mean (SE)	0.13 (0.22)	-0.07 (0.23)
95% CI of LS mean	(-0.31, 0.57)	(-0.52, 0.39)
P-value within Treatment	0.5565	0.7663
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.20 (-0.83, 0.43)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5364
Hedges' G (SE)		-0.08 (0.12)
Hedges' 95% CI		(-0.32, 0.17)
Hedges' P-value		0.5347

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	97	113
Mean (SD)	10.27 (3.52)	9.63 (3.46)
Week 4 (MMRM)		
n	98	109
LS mean (SE)	10.55 (0.36)	9.37 (0.34)
95% CI of LS mean	(9.84, 11.25)	(8.71, 10.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.17 (-2.14, -0.20)
Absolute Change at Week 4 (MMRM)		
n	92	108
LS mean (SE)	0.25 (0.24)	-0.30 (0.22)
95% CI of LS mean	(-0.22, 0.72)	(-0.74, 0.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.55 (-1.20, 0.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 24 (MMRM)		
n	97	106
LS mean (SE)	10.92 (0.37)	9.47 (0.35)
95% CI of LS mean	(10.19, 11.65)	(8.77, 10.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.45 (-2.46, -0.45)
Absolute Change at Week 24 (MMRM)		
n	91	105
LS mean (SE)	0.64 (0.27)	-0.11 (0.25)
95% CI of LS mean	(0.11, 1.17)	(-0.60, 0.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.75 (-1.47, -0.03)
Week 52		
n	97	102
Mean (SD)	10.21 (3.50)	9.09 (3.14)
Absolute Change at Week 52		
n	91	101
Mean (SD)	0.00 (2.26)	-0.44 (2.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52 (MMRM)		
n	93	102
LS mean (SE)	10.27 (0.33)	9.14 (0.32)
95% CI of LS mean	(9.61, 10.92)	(8.52, 9.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.12 (-2.03, -0.22)
Absolute Change at Week 52 (MMRM)		
n	87	101
LS mean (SE)	0.03 (0.26)	-0.46 (0.24)
95% CI of LS mean	(-0.49, 0.55)	(-0.94, 0.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.49 (-1.20, 0.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change through Week 52 (MMRM)		
n	92	106
LS mean (SE)	0.33 (0.23)	-0.29 (0.21)
95% CI of LS mean	(-0.11, 0.78)	(-0.70, 0.13)
P-value within Treatment	0.1423	0.1740
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.62 (-1.23, -0.01)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0465
Hedges' G (SE)		-0.29 (0.14)
Hedges' 95% CI		(-0.57, 0.00)
Hedges' P-value		0.0470

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	179	169
Mean (SD)	10.34 (3.40)	10.34 (3.71)
Week 4 (MMRM)		
n	175	158
LS mean (SE)	10.20 (0.27)	10.53 (0.29)
95% CI of LS mean	(9.67, 10.74)	(9.97, 11.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.33 (-0.45, 1.11)
Absolute Change at Week 4 (MMRM)		
n	169	158
LS mean (SE)	-0.18 (0.22)	0.17 (0.23)
95% CI of LS mean	(-0.61, 0.25)	(-0.27, 0.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-0.26, 0.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 24 (MMRM)		
n	169	151
LS mean (SE)	10.34 (0.29)	10.51 (0.30)
95% CI of LS mean	(9.78, 10.91)	(9.91, 11.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-0.65, 0.99)
Absolute Change at Week 24 (MMRM)		
n	163	150
LS mean (SE)	0.00 (0.24)	0.15 (0.25)
95% CI of LS mean	(-0.48, 0.48)	(-0.35, 0.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-0.54, 0.85)
Week 52		
n	176	156
Mean (SD)	9.89 (3.89)	9.90 (3.37)
Absolute Change at Week 52		
n	170	155
Mean (SD)	-0.45 (3.28)	-0.34 (2.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52 (MMRM)		
n	171	150
LS mean (SE)	9.89 (0.28)	9.97 (0.29)
95% CI of LS mean	(9.34, 10.43)	(9.40, 10.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.09 (-0.70, 0.88)
Absolute Change at Week 52 (MMRM)		
n	165	149
LS mean (SE)	-0.48 (0.24)	-0.34 (0.25)
95% CI of LS mean	(-0.95, 0.00)	(-0.85, 0.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-0.56, 0.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	170	156
LS mean (SE)	-0.24 (0.21)	-0.10 (0.22)
95% CI of LS mean	(-0.65, 0.17)	(-0.52, 0.33)
P-value within Treatment	0.2519	0.6579
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-0.45, 0.73)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6364
Hedges' G (SE)		0.05 (0.11)
Hedges' 95% CI		(-0.17, 0.27)
Hedges' P-value		0.6361

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	160	152
Mean (SD)	12.71 (4.81)	12.44 (4.48)
Week 4 (MMRM)		
n	158	145
LS mean (SE)	12.71 (0.39)	12.57 (0.41)
95% CI of LS mean	(11.94, 13.47)	(11.77, 13.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-1.25, 0.97)
Absolute Change at Week 4 (MMRM)		
n	152	144
LS mean (SE)	0.04 (0.36)	0.09 (0.37)
95% CI of LS mean	(-0.67, 0.76)	(-0.64, 0.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-0.97, 1.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 24 (MMRM)		
n	154	144
LS mean (SE)	13.27 (0.42)	12.37 (0.43)
95% CI of LS mean	(12.45, 14.09)	(11.52, 13.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.91 (-2.09, 0.28)
Absolute Change at Week 24 (MMRM)		
n	148	143
LS mean (SE)	0.54 (0.37)	-0.20 (0.38)
95% CI of LS mean	(-0.19, 1.27)	(-0.94, 0.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.74 (-1.78, 0.30)
Week 52		
n	156	141
Mean (SD)	12.87 (5.14)	11.44 (4.01)
Absolute Change at Week 52		
n	150	139
Mean (SD)	0.11 (4.44)	-0.76 (3.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52 (MMRM)		
n	151	140
LS mean (SE)	12.76 (0.37)	11.61 (0.38)
95% CI of LS mean	(12.04, 13.48)	(10.86, 12.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.15 (-2.19, -0.11)
Absolute Change at Week 52 (MMRM)		
n	145	138
LS mean (SE)	0.12 (0.33)	-0.83 (0.34)
95% CI of LS mean	(-0.53, 0.76)	(-1.49, -0.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.94 (-1.87, -0.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change through Week 52 (MMRM)		
n	151	144
LS mean (SE)	0.33 (0.29)	-0.51 (0.30)
95% CI of LS mean	(-0.24, 0.90)	(-1.09, 0.07)
P-value within Treatment	0.2552	0.0849
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.84 (-1.66, -0.03)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0432
Hedges' G (SE)		-0.24 (0.12)
Hedges' 95% CI		(-0.47, -0.01)
Hedges' P-value		0.0437

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	114	124
Mean (SD)	11.14 (4.20)	11.40 (3.69)
Week 4 (MMRM)		
n	115	119
LS mean (SE)	11.21 (0.43)	11.26 (0.42)
95% CI of LS mean	(10.36, 12.06)	(10.42, 12.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-1.14, 1.25)
Absolute Change at Week 4 (MMRM)		
n	110	118
LS mean (SE)	0.04 (0.36)	-0.15 (0.35)
95% CI of LS mean	(-0.68, 0.75)	(-0.83, 0.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-1.18, 0.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 24 (MMRM)		
n	113	115
LS mean (SE)	11.33 (0.42)	11.58 (0.42)
95% CI of LS mean	(10.49, 12.16)	(10.76, 12.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.25 (-0.92, 1.43)
Absolute Change at Week 24 (MMRM)		
n	108	114
LS mean (SE)	0.19 (0.35)	0.21 (0.34)
95% CI of LS mean	(-0.51, 0.88)	(-0.46, 0.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.02 (-0.94, 0.99)
Week 52		
n	115	114
Mean (SD)	11.09 (4.39)	10.79 (3.91)
Absolute Change at Week 52		
n	110	113
Mean (SD)	-0.05 (4.28)	-0.39 (2.79)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52 (MMRM)		
n	114	113
LS mean (SE)	11.14 (0.39)	10.93 (0.39)
95% CI of LS mean	(10.36, 11.91)	(10.16, 11.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.21 (-1.30, 0.89)
Absolute Change at Week 52 (MMRM)		
n	109	112
LS mean (SE)	0.07 (0.35)	-0.41 (0.35)
95% CI of LS mean	(-0.63, 0.76)	(-1.10, 0.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.48 (-1.46, 0.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change through Week 52 (MMRM)		
n	112	118
LS mean (SE)	0.13 (0.31)	-0.10 (0.30)
95% CI of LS mean	(-0.48, 0.73)	(-0.69, 0.49)
P-value within Treatment	0.6800	0.7369
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-1.08, 0.62)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5975
Hedges' G (SE)		-0.07 (0.13)
Hedges' 95% CI		(-0.33, 0.19)
Hedges' P-value		0.5962

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	34	40
Mean (SD)	9.97 (2.99)	10.83 (3.62)
Week 4 (MMRM)		
n	35	38
LS mean (SE)	9.73 (0.41)	9.79 (0.39)
95% CI of LS mean	(8.91, 10.54)	(9.01, 10.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.06 (-1.08, 1.19)
Absolute Change at Week 4 (MMRM)		
n	32	37
LS mean (SE)	-0.09 (0.38)	-0.88 (0.35)
95% CI of LS mean	(-0.84, 0.67)	(-1.58, -0.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.79 (-1.83, 0.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 24 (MMRM)		
n	33	33
LS mean (SE)	9.81 (0.55)	9.82 (0.54)
95% CI of LS mean	(8.72, 10.91)	(8.73, 10.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-1.54, 1.55)
Absolute Change at Week 24 (MMRM)		
n	30	32
LS mean (SE)	-0.08 (0.59)	-0.76 (0.56)
95% CI of LS mean	(-1.26, 1.09)	(-1.88, 0.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.68 (-2.31, 0.95)
Week 52		
n	35	36
Mean (SD)	9.20 (2.48)	9.58 (3.13)
Absolute Change at Week 52		
n	32	35
Mean (SD)	-0.59 (2.30)	-0.80 (3.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52 (MMRM)		
n	33	36
LS mean (SE)	9.21 (0.51)	9.72 (0.49)
95% CI of LS mean	(8.19, 10.22)	(8.75, 10.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.52 (-0.90, 1.93)
Absolute Change at Week 52 (MMRM)		
n	30	35
LS mean (SE)	-0.67 (0.47)	-0.89 (0.44)
95% CI of LS mean	(-1.61, 0.27)	(-1.77, -0.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-1.51, 1.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change through Week 52 (MMRM)		
n	31	35
LS mean (SE)	-0.38 (0.45)	-0.83 (0.42)
95% CI of LS mean	(-1.28, 0.53)	(-1.68, 0.02)
P-value within Treatment	0.4076	0.0557
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.45 (-1.69, 0.79)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4707
Hedges' G (SE)		-0.18 (0.24)
Hedges' 95% CI		(-0.67, 0.31)
Hedges' P-value		0.4699

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	243	241
Mean (SD)	12.31 (4.73)	12.20 (4.23)
Week 4 (MMRM)		
n	238	226
LS mean (SE)	12.43 (0.33)	12.33 (0.33)
95% CI of LS mean	(11.78, 13.07)	(11.67, 12.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-1.02, 0.82)
Absolute Change at Week 4 (MMRM)		
n	230	225
LS mean (SE)	0.05 (0.29)	0.13 (0.29)
95% CI of LS mean	(-0.52, 0.63)	(-0.45, 0.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-0.74, 0.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 24 (MMRM)		
n	234	226
LS mean (SE)	12.84 (0.33)	12.37 (0.34)
95% CI of LS mean	(12.18, 13.49)	(11.70, 13.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-1.41, 0.47)
Absolute Change at Week 24 (MMRM)		
n	226	225
LS mean (SE)	0.45 (0.28)	0.10 (0.28)
95% CI of LS mean	(-0.11, 1.01)	(-0.46, 0.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.35 (-1.14, 0.44)
Week 52		
n	239	223
Mean (SD)	12.52 (5.01)	11.41 (4.04)
Absolute Change at Week 52		
n	231	221
Mean (SD)	0.15 (4.55)	-0.57 (3.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52 (MMRM)		
n	232	217
LS mean (SE)	12.50 (0.30)	11.55 (0.31)
95% CI of LS mean	(11.91, 13.08)	(10.95, 12.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.94 (-1.79, -0.10)
Absolute Change at Week 52 (MMRM)		
n	224	215
LS mean (SE)	0.19 (0.26)	-0.61 (0.27)
95% CI of LS mean	(-0.33, 0.71)	(-1.13, -0.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.80 (-1.54, -0.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change through Week 52 (MMRM)		
n	232	227
LS mean (SE)	0.32 (0.23)	-0.25 (0.23)
95% CI of LS mean	(-0.13, 0.77)	(-0.71, 0.20)
P-value within Treatment	0.1646	0.2769
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.57 (-1.22, 0.07)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0807
Hedges' G (SE)		-0.16 (0.09)
Hedges' 95% CI		(-0.35, 0.02)
Hedges' P-value		0.0808

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	77	71
Mean (SD)	12.99 (5.57)	11.75 (4.13)
Week 4 (MMRM)		
n	77	67
LS mean (SE)	12.66 (0.57)	11.88 (0.61)
95% CI of LS mean	(11.54, 13.77)	(10.67, 13.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.78 (-2.43, 0.87)
Absolute Change at Week 4 (MMRM)		
n	74	66
LS mean (SE)	-0.38 (0.51)	0.07 (0.55)
95% CI of LS mean	(-1.40, 0.63)	(-1.01, 1.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-1.03, 1.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 24 (MMRM)		
n	76	62
LS mean (SE)	13.84 (0.59)	11.90 (0.65)
95% CI of LS mean	(12.67, 15.02)	(10.61, 13.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.95 (-3.69, -0.21)
Absolute Change at Week 24 (MMRM)		
n	73	61
LS mean (SE)	0.86 (0.50)	0.16 (0.54)
95% CI of LS mean	(-0.14, 1.85)	(-0.92, 1.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.69 (-2.16, 0.77)
Week 52		
n	78	64
Mean (SD)	12.35 (5.14)	11.42 (4.15)
Absolute Change at Week 52		
n	75	63
Mean (SD)	-0.65 (4.16)	0.17 (2.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52 (MMRM)		
n	77	61
LS mean (SE)	12.41 (0.52)	11.63 (0.58)
95% CI of LS mean	(11.37, 13.45)	(10.48, 12.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.78 (-2.33, 0.77)
Absolute Change at Week 52 (MMRM)		
n	74	60
LS mean (SE)	-0.53 (0.44)	0.06 (0.49)
95% CI of LS mean	(-1.41, 0.35)	(-0.91, 1.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-0.73, 1.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change through Week 52 (MMRM)		
n	75	63
LS mean (SE)	0.16 (0.40)	0.11 (0.43)
95% CI of LS mean	(-0.62, 0.95)	(-0.75, 0.97)
P-value within Treatment	0.6796	0.8010
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-1.22, 1.11)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9255
Hedges' G (SE)		-0.02 (0.17)
Hedges' 95% CI		(-0.35, 0.32)
Hedges' P-value		0.9253

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	193	208
Mean (SD)	11.65 (4.14)	12.12 (4.20)
Week 4 (MMRM)		
n	196	197
LS mean (SE)	11.85 (0.34)	12.00 (0.33)
95% CI of LS mean	(11.18, 12.51)	(11.35, 12.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-0.78, 1.09)
Absolute Change at Week 4 (MMRM)		
n	188	196
LS mean (SE)	0.21 (0.30)	-0.03 (0.29)
95% CI of LS mean	(-0.38, 0.79)	(-0.61, 0.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-1.06, 0.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 24 (MMRM)		
n	191	197
LS mean (SE)	11.90 (0.34)	12.05 (0.34)
95% CI of LS mean	(11.23, 12.58)	(11.38, 12.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-0.81, 1.09)
Absolute Change at Week 24 (MMRM)		
n	183	196
LS mean (SE)	0.21 (0.30)	-0.07 (0.29)
95% CI of LS mean	(-0.39, 0.80)	(-0.65, 0.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.28 (-1.11, 0.55)
Week 52		
n	190	193
Mean (SD)	12.02 (4.79)	11.09 (3.92)
Absolute Change at Week 52		
n	182	191
Mean (SD)	0.35 (4.46)	-0.86 (3.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52 (MMRM)		
n	188	192
LS mean (SE)	11.96 (0.31)	11.19 (0.31)
95% CI of LS mean	(11.35, 12.57)	(10.58, 11.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.77 (-1.63, 0.09)
Absolute Change at Week 52 (MMRM)		
n	180	190
LS mean (SE)	0.34 (0.28)	-0.86 (0.27)
95% CI of LS mean	(-0.21, 0.89)	(-1.40, -0.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.20 (-1.97, -0.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change through Week 52 (MMRM)		
n	188	199
LS mean (SE)	0.27 (0.25)	-0.47 (0.24)
95% CI of LS mean	(-0.21, 0.76)	(-0.93, 0.00)
P-value within Treatment	0.2659	0.0508
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.74 (-1.41, -0.07)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0312
Hedges' G (SE)		-0.22 (0.10)
Hedges' 95% CI		(-0.42, -0.02)
Hedges' P-value		0.0316

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	139	147
Mean (SD)	11.47 (4.21)	11.43 (4.06)
Week 4 (MMRM)		
n	132	138
LS mean (SE)	11.42 (0.38)	11.39 (0.37)
95% CI of LS mean	(10.67, 12.18)	(10.65, 12.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-1.10, 1.03)
Absolute Change at Week 4 (MMRM)		
n	128	136
LS mean (SE)	-0.07 (0.36)	0.00 (0.35)
95% CI of LS mean	(-0.78, 0.64)	(-0.69, 0.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-0.93, 1.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 24 (MMRM)		
n	130	138
LS mean (SE)	11.81 (0.37)	10.85 (0.36)
95% CI of LS mean	(11.08, 12.54)	(10.14, 11.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.96 (-1.98, 0.06)
Absolute Change at Week 24 (MMRM)		
n	126	137
LS mean (SE)	0.37 (0.34)	-0.61 (0.33)
95% CI of LS mean	(-0.30, 1.04)	(-1.26, 0.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.98 (-1.91, -0.04)
Week 52		
n	138	140
Mean (SD)	11.77 (4.92)	10.59 (3.73)
Absolute Change at Week 52		
n	134	138
Mean (SD)	0.35 (4.18)	-0.74 (2.89)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52 (MMRM)		
n	130	136
LS mean (SE)	11.80 (0.37)	10.59 (0.36)
95% CI of LS mean	(11.06, 12.53)	(9.87, 11.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.21 (-2.25, -0.18)
Absolute Change at Week 52 (MMRM)		
n	126	134
LS mean (SE)	0.41 (0.32)	-0.84 (0.31)
95% CI of LS mean	(-0.22, 1.04)	(-1.45, -0.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.25 (-2.13, -0.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change through Week 52 (MMRM)		
n	129	138
LS mean (SE)	0.39 (0.28)	-0.73 (0.27)
95% CI of LS mean	(-0.17, 0.94)	(-1.26, -0.19)
P-value within Treatment	0.1728	0.0083
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.11 (-1.89, -0.33)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0053
Hedges' G (SE)		-0.35 (0.12)
Hedges' 95% CI		(-0.59, -0.10)
Hedges' P-value		0.0053

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	138	134
Mean (SD)	12.59 (4.93)	12.63 (4.22)
Week 4 (MMRM)		
n	141	126
LS mean (SE)	12.65 (0.43)	12.66 (0.45)
95% CI of LS mean	(11.80, 13.50)	(11.77, 13.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-1.23, 1.25)
Absolute Change at Week 4 (MMRM)		
n	134	126
LS mean (SE)	0.20 (0.37)	-0.08 (0.38)
95% CI of LS mean	(-0.53, 0.93)	(-0.83, 0.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.28 (-1.33, 0.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 24 (MMRM)		
n	137	121
LS mean (SE)	13.04 (0.46)	13.37 (0.49)
95% CI of LS mean	(12.13, 13.95)	(12.40, 14.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.33 (-1.01, 1.66)
Absolute Change at Week 24 (MMRM)		
n	130	120
LS mean (SE)	0.50 (0.40)	0.60 (0.41)
95% CI of LS mean	(-0.28, 1.28)	(-0.21, 1.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.11 (-1.02, 1.23)
Week 52		
n	136	119
Mean (SD)	12.43 (4.85)	11.82 (4.15)
Absolute Change at Week 52		
n	129	118
Mean (SD)	-0.25 (4.50)	-0.45 (3.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52 (MMRM)		
n	135	117
LS mean (SE)	12.30 (0.39)	12.11 (0.41)
95% CI of LS mean	(11.53, 13.06)	(11.30, 12.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.19 (-1.31, 0.93)
Absolute Change at Week 52 (MMRM)		
n	128	116
LS mean (SE)	-0.15 (0.36)	-0.51 (0.37)
95% CI of LS mean	(-0.85, 0.55)	(-1.24, 0.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.36 (-1.38, 0.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change through Week 52 (MMRM)		
n	134	124
LS mean (SE)	0.17 (0.31)	0.05 (0.32)
95% CI of LS mean	(-0.44, 0.79)	(-0.59, 0.68)
P-value within Treatment	0.5782	0.8862
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-1.02, 0.76)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7781
Hedges' G (SE)		-0.04 (0.12)
Hedges' 95% CI		(-0.28, 0.21)
Hedges' P-value		0.7770

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	98	112
Mean (SD)	11.96 (4.62)	11.71 (3.90)
Week 4 (MMRM)		
n	98	110
LS mean (SE)	12.15 (0.44)	11.39 (0.41)
95% CI of LS mean	(11.29, 13.02)	(10.57, 12.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.76 (-1.96, 0.43)
Absolute Change at Week 4 (MMRM)		
n	93	108
LS mean (SE)	0.27 (0.31)	-0.31 (0.29)
95% CI of LS mean	(-0.35, 0.89)	(-0.89, 0.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.59 (-1.43, 0.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 24 (MMRM)		
n	97	106
LS mean (SE)	12.42 (0.46)	11.18 (0.43)
95% CI of LS mean	(11.52, 13.32)	(10.33, 12.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.24 (-2.48, 0.01)
Absolute Change at Week 24 (MMRM)		
n	92	105
LS mean (SE)	0.47 (0.32)	-0.50 (0.30)
95% CI of LS mean	(-0.17, 1.11)	(-1.10, 0.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.97 (-1.85, -0.09)
Week 52		
n	97	102
Mean (SD)	12.13 (4.71)	10.65 (3.40)
Absolute Change at Week 52		
n	92	100
Mean (SD)	0.23 (2.70)	-1.00 (2.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52 (MMRM)		
n	93	102
LS mean (SE)	12.10 (0.40)	10.74 (0.38)
95% CI of LS mean	(11.30, 12.90)	(9.98, 11.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.37 (-2.47, -0.26)
Absolute Change at Week 52 (MMRM)		
n	88	100
LS mean (SE)	0.26 (0.30)	-0.97 (0.28)
95% CI of LS mean	(-0.33, 0.84)	(-1.51, -0.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.22 (-2.03, -0.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change through Week 52 (MMRM)		
n	93	105
LS mean (SE)	0.36 (0.27)	-0.73 (0.25)
95% CI of LS mean	(-0.17, 0.90)	(-1.23, -0.23)
P-value within Treatment	0.1823	0.0043
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.10 (-1.83, -0.36)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0036
Hedges' G (SE)		-0.42 (0.14)
Hedges' 95% CI		(-0.70, -0.14)
Hedges' P-value		0.0039

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	179	169
Mean (SD)	12.06 (4.62)	12.20 (4.34)
Week 4 (MMRM)		
n	175	154
LS mean (SE)	12.04 (0.38)	12.37 (0.40)
95% CI of LS mean	(11.29, 12.79)	(11.57, 13.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.33 (-0.77, 1.42)
Absolute Change at Week 4 (MMRM)		
n	169	154
LS mean (SE)	-0.11 (0.37)	0.22 (0.38)
95% CI of LS mean	(-0.84, 0.61)	(-0.54, 0.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.33 (-0.72, 1.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 24 (MMRM)		
n	170	153
LS mean (SE)	12.47 (0.39)	12.57 (0.41)
95% CI of LS mean	(11.70, 13.24)	(11.75, 13.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-1.02, 1.22)
Absolute Change at Week 24 (MMRM)		
n	164	152
LS mean (SE)	0.31 (0.36)	0.34 (0.38)
95% CI of LS mean	(-0.40, 1.03)	(-0.40, 1.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.03 (-1.00, 1.06)
Week 52		
n	177	157
Mean (SD)	12.07 (4.99)	11.48 (4.28)
Absolute Change at Week 52		
n	171	156
Mean (SD)	-0.04 (5.02)	-0.35 (3.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52 (MMRM)		
n	172	151
LS mean (SE)	12.05 (0.35)	11.67 (0.37)
95% CI of LS mean	(11.36, 12.75)	(10.93, 12.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-1.40, 0.63)
Absolute Change at Week 52 (MMRM)		
n	166	150
LS mean (SE)	-0.03 (0.34)	-0.40 (0.35)
95% CI of LS mean	(-0.69, 0.63)	(-1.09, 0.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.36 (-1.32, 0.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Physical Activity
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	170	157
LS mean (SE)	0.14 (0.29)	-0.03 (0.30)
95% CI of LS mean	(-0.43, 0.71)	(-0.62, 0.57)
P-value within Treatment	0.6278	0.9314
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-1.00, 0.66)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6911
Hedges' G (SE)		-0.04 (0.11)
Hedges' 95% CI		(-0.26, 0.17)
Hedges' P-value		0.6908

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	160	153
Mean (SD)	5.71 (2.76)	5.31 (2.04)
Week 4 (MMRM)		
n	158	146
LS mean (SE)	5.70 (0.19)	5.35 (0.20)
95% CI of LS mean	(5.32, 6.08)	(4.96, 5.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.35 (-0.90, 0.19)
Absolute Change at Week 4 (MMRM)		
n	152	146
LS mean (SE)	0.05 (0.16)	0.00 (0.17)
95% CI of LS mean	(-0.27, 0.37)	(-0.33, 0.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-0.51, 0.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 24 (MMRM)		
n	154	144
LS mean (SE)	5.67 (0.19)	5.14 (0.20)
95% CI of LS mean	(5.29, 6.05)	(4.74, 5.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.53 (-1.08, 0.01)
Absolute Change at Week 24 (MMRM)		
n	148	143
LS mean (SE)	-0.02 (0.18)	-0.24 (0.18)
95% CI of LS mean	(-0.37, 0.33)	(-0.60, 0.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-0.72, 0.28)
Week 52		
n	156	141
Mean (SD)	5.49 (2.61)	5.01 (1.85)
Absolute Change at Week 52		
n	150	140
Mean (SD)	-0.29 (2.14)	-0.25 (1.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52 (MMRM)		
n	151	140
LS mean (SE)	5.43 (0.18)	5.09 (0.19)
95% CI of LS mean	(5.07, 5.79)	(4.72, 5.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.34 (-0.85, 0.18)
Absolute Change at Week 52 (MMRM)		
n	145	139
LS mean (SE)	-0.29 (0.16)	-0.25 (0.16)
95% CI of LS mean	(-0.60, 0.02)	(-0.57, 0.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.04 (-0.40, 0.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change through Week 52 (MMRM)		
n	151	145
LS mean (SE)	-0.16 (0.15)	-0.25 (0.15)
95% CI of LS mean	(-0.44, 0.13)	(-0.54, 0.04)
P-value within Treatment	0.2857	0.0965
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.50, 0.32)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6603
Hedges' G (SE)		-0.05 (0.12)
Hedges' 95% CI		(-0.28, 0.18)
Hedges' P-value		0.6600

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	115	124
Mean (SD)	4.96 (1.70)	5.31 (2.09)
Week 4 (MMRM)		
n	115	120
LS mean (SE)	5.22 (0.21)	5.34 (0.21)
95% CI of LS mean	(4.81, 5.64)	(4.94, 5.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-0.46, 0.70)
Absolute Change at Week 4 (MMRM)		
n	111	119
LS mean (SE)	0.28 (0.19)	0.03 (0.18)
95% CI of LS mean	(-0.09, 0.66)	(-0.33, 0.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-0.77, 0.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 24 (MMRM)		
n	113	114
LS mean (SE)	5.23 (0.21)	5.05 (0.21)
95% CI of LS mean	(4.83, 5.64)	(4.65, 5.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-0.76, 0.39)
Absolute Change at Week 24 (MMRM)		
n	109	113
LS mean (SE)	0.32 (0.18)	-0.22 (0.18)
95% CI of LS mean	(-0.04, 0.68)	(-0.58, 0.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.54 (-1.05, -0.03)
Week 52		
n	115	114
Mean (SD)	4.96 (2.02)	4.89 (1.58)
Absolute Change at Week 52		
n	111	113
Mean (SD)	0.00 (1.76)	-0.35 (1.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52 (MMRM)		
n	114	113
LS mean (SE)	4.95 (0.17)	4.90 (0.17)
95% CI of LS mean	(4.61, 5.28)	(4.57, 5.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-0.52, 0.43)
Absolute Change at Week 52 (MMRM)		
n	110	112
LS mean (SE)	0.03 (0.16)	-0.38 (0.16)
95% CI of LS mean	(-0.29, 0.34)	(-0.69, -0.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.41 (-0.86, 0.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change through Week 52 (MMRM)		
n	113	118
LS mean (SE)	0.17 (0.14)	-0.30 (0.14)
95% CI of LS mean	(-0.11, 0.46)	(-0.58, -0.02)
P-value within Treatment	0.2313	0.0334
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.48 (-0.88, -0.08)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0198
Hedges' G (SE)		-0.31 (0.13)
Hedges' 95% CI		(-0.57, -0.05)
Hedges' P-value		0.0201

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	35	40
Mean (SD)	4.74 (1.24)	5.30 (1.83)
Week 4 (MMRM)		
n	35	39
LS mean (SE)	5.12 (0.24)	4.87 (0.23)
95% CI of LS mean	(4.63, 5.60)	(4.41, 5.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-0.92, 0.43)
Absolute Change at Week 4 (MMRM)		
n	33	38
LS mean (SE)	0.43 (0.23)	-0.32 (0.21)
95% CI of LS mean	(-0.02, 0.89)	(-0.75, 0.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.76 (-1.38, -0.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 24 (MMRM)		
n	33	32
LS mean (SE)	4.72 (0.20)	4.40 (0.20)
95% CI of LS mean	(4.32, 5.11)	(4.00, 4.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.32 (-0.89, 0.25)
Absolute Change at Week 24 (MMRM)		
n	31	31
LS mean (SE)	0.17 (0.23)	-0.73 (0.23)
95% CI of LS mean	(-0.30, 0.64)	(-1.19, -0.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.90 (-1.56, -0.23)
Week 52		
n	35	36
Mean (SD)	4.69 (1.23)	4.53 (1.00)
Absolute Change at Week 52		
n	33	35
Mean (SD)	0.03 (1.07)	-0.46 (1.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52 (MMRM)		
n	33	36
LS mean (SE)	4.65 (0.20)	4.64 (0.20)
95% CI of LS mean	(4.24, 5.06)	(4.24, 5.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.01 (-0.58, 0.55)
Absolute Change at Week 52 (MMRM)		
n	31	35
LS mean (SE)	0.03 (0.22)	-0.47 (0.20)
95% CI of LS mean	(-0.40, 0.46)	(-0.88, -0.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.50 (-1.10, 0.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change through Week 52 (MMRM)		
n	32	35
LS mean (SE)	0.10 (0.21)	-0.60 (0.20)
95% CI of LS mean	(-0.31, 0.51)	(-1.00, -0.20)
P-value within Treatment	0.6314	0.0038
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.70 (-1.28, -0.12)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0185
Hedges' G (SE)		-0.59 (0.25)
Hedges' 95% CI		(-1.08, -0.10)
Hedges' P-value		0.0201

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	243	242
Mean (SD)	5.47 (2.50)	5.33 (2.10)
Week 4 (MMRM)		
n	238	227
LS mean (SE)	5.57 (0.16)	5.41 (0.16)
95% CI of LS mean	(5.26, 5.88)	(5.09, 5.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.16 (-0.61, 0.29)
Absolute Change at Week 4 (MMRM)		
n	230	227
LS mean (SE)	0.10 (0.14)	0.07 (0.14)
95% CI of LS mean	(-0.17, 0.37)	(-0.20, 0.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-0.41, 0.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 24 (MMRM)		
n	234	226
LS mean (SE)	5.61 (0.16)	5.20 (0.16)
95% CI of LS mean	(5.29, 5.92)	(4.88, 5.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.41 (-0.85, 0.04)
Absolute Change at Week 24 (MMRM)		
n	226	225
LS mean (SE)	0.12 (0.14)	-0.16 (0.14)
95% CI of LS mean	(-0.16, 0.40)	(-0.45, 0.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.28 (-0.68, 0.12)
Week 52		
n	239	223
Mean (SD)	5.34 (2.49)	5.01 (1.81)
Absolute Change at Week 52		
n	231	222
Mean (SD)	-0.19 (2.07)	-0.29 (1.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52 (MMRM)		
n	232	217
LS mean (SE)	5.32 (0.14)	5.05 (0.15)
95% CI of LS mean	(5.04, 5.60)	(4.77, 5.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.27 (-0.67, 0.14)
Absolute Change at Week 52 (MMRM)		
n	224	216
LS mean (SE)	-0.18 (0.12)	-0.28 (0.13)
95% CI of LS mean	(-0.43, 0.06)	(-0.53, -0.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-0.44, 0.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change through Week 52 (MMRM)		
n	232	228
LS mean (SE)	-0.03 (0.11)	-0.22 (0.12)
95% CI of LS mean	(-0.26, 0.19)	(-0.45, 0.01)
P-value within Treatment	0.7810	0.0570
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.19 (-0.51, 0.13)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2479
Hedges' G (SE)		-0.11 (0.09)
Hedges' 95% CI		(-0.29, 0.08)
Hedges' P-value		0.2476

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	78	71
Mean (SD)	5.72 (2.77)	5.32 (2.11)
Week 4 (MMRM)		
n	77	67
LS mean (SE)	6.07 (0.29)	5.26 (0.32)
95% CI of LS mean	(5.49, 6.65)	(4.64, 5.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.81 (-1.66, 0.05)
Absolute Change at Week 4 (MMRM)		
n	75	66
LS mean (SE)	0.32 (0.25)	-0.01 (0.26)
95% CI of LS mean	(-0.17, 0.81)	(-0.54, 0.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-1.05, 0.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 24 (MMRM)		
n	76	62
LS mean (SE)	6.17 (0.29)	4.97 (0.32)
95% CI of LS mean	(5.59, 6.75)	(4.33, 5.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.20 (-2.06, -0.34)
Absolute Change at Week 24 (MMRM)		
n	74	61
LS mean (SE)	0.46 (0.29)	-0.27 (0.32)
95% CI of LS mean	(-0.11, 1.03)	(-0.90, 0.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.73 (-1.59, 0.12)
Week 52		
n	78	64
Mean (SD)	5.47 (2.63)	4.75 (1.58)
Absolute Change at Week 52		
n	76	63
Mean (SD)	-0.24 (1.99)	-0.29 (1.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52 (MMRM)		
n	77	61
LS mean (SE)	5.48 (0.26)	4.84 (0.28)
95% CI of LS mean	(4.98, 5.99)	(4.28, 5.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-1.40, 0.12)
Absolute Change at Week 52 (MMRM)		
n	75	60
LS mean (SE)	-0.23 (0.22)	-0.30 (0.25)
95% CI of LS mean	(-0.66, 0.21)	(-0.78, 0.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-0.73, 0.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change through Week 52 (MMRM)		
n	76	63
LS mean (SE)	0.12 (0.22)	-0.29 (0.24)
95% CI of LS mean	(-0.32, 0.55)	(-0.76, 0.19)
P-value within Treatment	0.5931	0.2393
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.40 (-1.05, 0.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2201
Hedges' G (SE)		-0.21 (0.17)
Hedges' 95% CI		(-0.55, 0.13)
Hedges' P-value		0.2204

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	193	209
Mean (SD)	5.22 (2.20)	5.33 (2.05)
Week 4 (MMRM)		
n	196	199
LS mean (SE)	5.29 (0.16)	5.36 (0.16)
95% CI of LS mean	(4.97, 5.60)	(5.05, 5.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-0.37, 0.51)
Absolute Change at Week 4 (MMRM)		
n	188	199
LS mean (SE)	0.07 (0.14)	0.03 (0.14)
95% CI of LS mean	(-0.21, 0.35)	(-0.24, 0.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-0.43, 0.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 24 (MMRM)		
n	191	196
LS mean (SE)	5.22 (0.16)	5.13 (0.15)
95% CI of LS mean	(4.91, 5.53)	(4.83, 5.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.53, 0.34)
Absolute Change at Week 24 (MMRM)		
n	183	195
LS mean (SE)	-0.02 (0.14)	-0.22 (0.14)
95% CI of LS mean	(-0.29, 0.26)	(-0.48, 0.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.20 (-0.58, 0.18)
Week 52		
n	190	193
Mean (SD)	5.15 (2.24)	5.00 (1.77)
Absolute Change at Week 52		
n	182	192
Mean (SD)	-0.13 (2.00)	-0.34 (1.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52 (MMRM)		
n	188	192
LS mean (SE)	5.14 (0.15)	5.05 (0.14)
95% CI of LS mean	(4.85, 5.42)	(4.77, 5.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.49, 0.31)
Absolute Change at Week 52 (MMRM)		
n	180	191
LS mean (SE)	-0.13 (0.13)	-0.30 (0.13)
95% CI of LS mean	(-0.39, 0.13)	(-0.55, -0.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-0.53, 0.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change through Week 52 (MMRM)		
n	188	200
LS mean (SE)	-0.07 (0.12)	-0.26 (0.11)
95% CI of LS mean	(-0.30, 0.16)	(-0.48, -0.03)
P-value within Treatment	0.5325	0.0239
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-0.51, 0.14)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2596
Hedges' G (SE)		-0.11 (0.10)
Hedges' 95% CI		(-0.31, 0.08)
Hedges' P-value		0.2597

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	139	148
Mean (SD)	5.27 (2.14)	5.07 (1.86)
Week 4 (MMRM)		
n	132	140
LS mean (SE)	5.38 (0.18)	5.16 (0.18)
95% CI of LS mean	(5.02, 5.74)	(4.81, 5.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-0.73, 0.29)
Absolute Change at Week 4 (MMRM)		
n	128	139
LS mean (SE)	0.13 (0.16)	0.07 (0.15)
95% CI of LS mean	(-0.17, 0.44)	(-0.22, 0.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-0.49, 0.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 24 (MMRM)		
n	130	138
LS mean (SE)	5.34 (0.18)	4.84 (0.18)
95% CI of LS mean	(4.99, 5.70)	(4.49, 5.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.50 (-1.00, 0.00)
Absolute Change at Week 24 (MMRM)		
n	126	137
LS mean (SE)	0.11 (0.15)	-0.24 (0.15)
95% CI of LS mean	(-0.19, 0.41)	(-0.53, 0.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.35 (-0.76, 0.07)
Week 52		
n	138	140
Mean (SD)	5.27 (2.37)	4.89 (1.85)
Absolute Change at Week 52		
n	134	139
Mean (SD)	-0.04 (1.92)	-0.12 (1.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52 (MMRM)		
n	130	136
LS mean (SE)	5.27 (0.19)	4.95 (0.18)
95% CI of LS mean	(4.90, 5.64)	(4.59, 5.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.32 (-0.84, 0.20)
Absolute Change at Week 52 (MMRM)		
n	126	135
LS mean (SE)	-0.02 (0.15)	-0.11 (0.14)
95% CI of LS mean	(-0.32, 0.27)	(-0.39, 0.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-0.50, 0.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change through Week 52 (MMRM)		
n	129	139
LS mean (SE)	0.04 (0.13)	-0.17 (0.12)
95% CI of LS mean	(-0.21, 0.29)	(-0.41, 0.07)
P-value within Treatment	0.7413	0.1551
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.21 (-0.56, 0.13)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2244
Hedges' G (SE)		-0.15 (0.12)
Hedges' 95% CI		(-0.39, 0.09)
Hedges' P-value		0.2217

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	139	134
Mean (SD)	5.49 (2.62)	5.60 (2.23)
Week 4 (MMRM)		
n	141	126
LS mean (SE)	5.63 (0.22)	5.54 (0.23)
95% CI of LS mean	(5.20, 6.05)	(5.09, 5.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.71, 0.54)
Absolute Change at Week 4 (MMRM)		
n	135	126
LS mean (SE)	0.17 (0.19)	-0.06 (0.20)
95% CI of LS mean	(-0.21, 0.54)	(-0.45, 0.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-0.77, 0.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 24 (MMRM)		
n	137	120
LS mean (SE)	5.63 (0.22)	5.38 (0.23)
95% CI of LS mean	(5.21, 6.06)	(4.93, 5.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-0.87, 0.38)
Absolute Change at Week 24 (MMRM)		
n	131	119
LS mean (SE)	0.15 (0.21)	-0.23 (0.22)
95% CI of LS mean	(-0.27, 0.56)	(-0.67, 0.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-0.98, 0.22)
Week 52		
n	136	119
Mean (SD)	5.24 (2.40)	5.01 (1.56)
Absolute Change at Week 52		
n	130	118
Mean (SD)	-0.28 (2.03)	-0.54 (1.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52 (MMRM)		
n	135	117
LS mean (SE)	5.20 (0.17)	5.05 (0.18)
95% CI of LS mean	(4.85, 5.54)	(4.68, 5.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-0.65, 0.35)
Absolute Change at Week 52 (MMRM)		
n	129	116
LS mean (SE)	-0.27 (0.17)	-0.55 (0.18)
95% CI of LS mean	(-0.60, 0.06)	(-0.90, -0.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.28 (-0.76, 0.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change through Week 52 (MMRM)		
n	135	124
LS mean (SE)	-0.06 (0.17)	-0.39 (0.17)
95% CI of LS mean	(-0.39, 0.27)	(-0.73, -0.05)
P-value within Treatment	0.7097	0.0247
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-0.81, 0.15)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1734
Hedges' G (SE)		-0.17 (0.12)
Hedges' 95% CI		(-0.41, 0.07)
Hedges' P-value		0.1722

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	99	113
Mean (SD)	5.51 (2.46)	5.09 (1.88)
Week 4 (MMRM)		
n	98	110
LS mean (SE)	5.81 (0.22)	5.01 (0.21)
95% CI of LS mean	(5.38, 6.25)	(4.60, 5.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.81 (-1.40, -0.21)
Absolute Change at Week 4 (MMRM)		
n	94	109
LS mean (SE)	0.26 (0.17)	-0.10 (0.15)
95% CI of LS mean	(-0.07, 0.59)	(-0.40, 0.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.36 (-0.81, 0.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 24 (MMRM)		
n	97	106
LS mean (SE)	5.63 (0.23)	4.93 (0.21)
95% CI of LS mean	(5.19, 6.08)	(4.51, 5.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.70 (-1.32, -0.09)
Absolute Change at Week 24 (MMRM)		
n	93	105
LS mean (SE)	0.14 (0.21)	-0.15 (0.19)
95% CI of LS mean	(-0.26, 0.55)	(-0.54, 0.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-0.85, 0.26)
Week 52		
n	97	102
Mean (SD)	5.33 (2.00)	4.79 (1.80)
Absolute Change at Week 52		
n	93	101
Mean (SD)	-0.23 (1.69)	-0.25 (1.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52 (MMRM)		
n	93	102
LS mean (SE)	5.31 (0.19)	4.85 (0.18)
95% CI of LS mean	(4.93, 5.70)	(4.49, 5.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.46 (-0.99, 0.07)
Absolute Change at Week 52 (MMRM)		
n	89	101
LS mean (SE)	-0.23 (0.15)	-0.22 (0.14)
95% CI of LS mean	(-0.53, 0.07)	(-0.51, 0.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-0.41, 0.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change through Week 52 (MMRM)		
n	94	106
LS mean (SE)	-0.04 (0.16)	-0.19 (0.15)
95% CI of LS mean	(-0.35, 0.26)	(-0.48, 0.10)
P-value within Treatment	0.7810	0.1956
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-0.57, 0.28)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4954
Hedges' G (SE)		-0.10 (0.14)
Hedges' 95% CI		(-0.38, 0.18)
Hedges' P-value		0.4947

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	179	169
Mean (SD)	5.31 (2.35)	5.48 (2.16)
Week 4 (MMRM)		
n	175	156
LS mean (SE)	5.34 (0.18)	5.56 (0.19)
95% CI of LS mean	(4.98, 5.70)	(5.18, 5.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.22 (-0.30, 0.75)
Absolute Change at Week 4 (MMRM)		
n	169	156
LS mean (SE)	0.07 (0.17)	0.10 (0.18)
95% CI of LS mean	(-0.26, 0.40)	(-0.25, 0.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.03 (-0.45, 0.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 24 (MMRM)		
n	170	152
LS mean (SE)	5.42 (0.18)	5.21 (0.19)
95% CI of LS mean	(5.06, 5.78)	(4.83, 5.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.21 (-0.73, 0.31)
Absolute Change at Week 24 (MMRM)		
n	164	151
LS mean (SE)	0.10 (0.17)	-0.28 (0.17)
95% CI of LS mean	(-0.22, 0.43)	(-0.62, 0.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-0.86, 0.09)
Week 52		
n	177	157
Mean (SD)	5.21 (2.56)	5.04 (1.67)
Absolute Change at Week 52		
n	171	156
Mean (SD)	-0.12 (2.12)	-0.36 (1.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52 (MMRM)		
n	172	151
LS mean (SE)	5.19 (0.17)	5.09 (0.18)
95% CI of LS mean	(4.86, 5.51)	(4.75, 5.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.57, 0.38)
Absolute Change at Week 52 (MMRM)		
n	166	150
LS mean (SE)	-0.12 (0.15)	-0.36 (0.16)
95% CI of LS mean	(-0.43, 0.18)	(-0.68, -0.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-0.67, 0.21)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Social Activity
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	170	157
LS mean (SE)	-0.01 (0.14)	-0.32 (0.14)
95% CI of LS mean	(-0.28, 0.26)	(-0.60, -0.04)
P-value within Treatment	0.9359	0.0268
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-0.70, 0.08)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1226
Hedges' G (SE)		-0.17 (0.11)
Hedges' 95% CI		(-0.39, 0.05)
Hedges' P-value		0.1229

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	160	152
Mean (SD)	7.11 (3.18)	6.95 (2.97)
Week 4 (MMRM)		
n	158	147
LS mean (SE)	7.17 (0.23)	6.73 (0.24)
95% CI of LS mean	(6.72, 7.62)	(6.26, 7.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.44 (-1.09, 0.21)
Absolute Change at Week 4 (MMRM)		
n	153	147
LS mean (SE)	0.09 (0.16)	-0.32 (0.17)
95% CI of LS mean	(-0.24, 0.41)	(-0.64, 0.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.40 (-0.86, 0.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 24 (MMRM)		
n	153	144
LS mean (SE)	7.00 (0.24)	7.04 (0.25)
95% CI of LS mean	(6.53, 7.47)	(6.55, 7.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.04 (-0.64, 0.72)
Absolute Change at Week 24 (MMRM)		
n	148	142
LS mean (SE)	-0.12 (0.20)	-0.03 (0.21)
95% CI of LS mean	(-0.52, 0.28)	(-0.44, 0.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.09 (-0.49, 0.67)
Week 52		
n	156	141
Mean (SD)	7.16 (3.25)	6.83 (3.00)
Absolute Change at Week 52		
n	150	139
Mean (SD)	-0.03 (2.84)	-0.09 (2.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52 (MMRM)		
n	151	140
LS mean (SE)	7.11 (0.25)	6.94 (0.26)
95% CI of LS mean	(6.62, 7.60)	(6.43, 7.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-0.88, 0.54)
Absolute Change at Week 52 (MMRM)		
n	146	138
LS mean (SE)	-0.01 (0.22)	-0.14 (0.23)
95% CI of LS mean	(-0.45, 0.43)	(-0.59, 0.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-0.76, 0.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change through Week 52 (MMRM)		
n	152	144
LS mean (SE)	-0.07 (0.19)	-0.09 (0.20)
95% CI of LS mean	(-0.44, 0.31)	(-0.47, 0.30)
P-value within Treatment	0.7226	0.6610
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.02 (-0.56, 0.52)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9473
Hedges' G (SE)		-0.01 (0.12)
Hedges' 95% CI		(-0.24, 0.22)
Hedges' P-value		0.9473

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	115	123
Mean (SD)	6.75 (2.46)	7.02 (2.66)
Week 4 (MMRM)		
n	117	122
LS mean (SE)	6.67 (0.25)	6.97 (0.24)
95% CI of LS mean	(6.18, 7.16)	(6.49, 7.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.29 (-0.39, 0.98)
Absolute Change at Week 4 (MMRM)		
n	113	120
LS mean (SE)	-0.09 (0.22)	-0.06 (0.21)
95% CI of LS mean	(-0.52, 0.33)	(-0.47, 0.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.03 (-0.56, 0.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 24 (MMRM)		
n	116	116
LS mean (SE)	6.74 (0.28)	7.15 (0.27)
95% CI of LS mean	(6.19, 7.28)	(6.62, 7.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.42 (-0.35, 1.18)
Absolute Change at Week 24 (MMRM)		
n	112	114
LS mean (SE)	-0.02 (0.26)	0.16 (0.26)
95% CI of LS mean	(-0.53, 0.49)	(-0.35, 0.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-0.54, 0.90)
Week 52		
n	115	114
Mean (SD)	6.59 (2.62)	6.75 (2.68)
Absolute Change at Week 52		
n	111	112
Mean (SD)	-0.16 (2.85)	-0.16 (2.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52 (MMRM)		
n	114	113
LS mean (SE)	6.65 (0.25)	6.75 (0.25)
95% CI of LS mean	(6.16, 7.14)	(6.27, 7.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-0.59, 0.80)
Absolute Change at Week 52 (MMRM)		
n	110	111
LS mean (SE)	-0.07 (0.26)	-0.22 (0.26)
95% CI of LS mean	(-0.58, 0.44)	(-0.72, 0.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-0.86, 0.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change through Week 52 (MMRM)		
n	113	117
LS mean (SE)	-0.05 (0.23)	-0.03 (0.23)
95% CI of LS mean	(-0.50, 0.41)	(-0.47, 0.42)
P-value within Treatment	0.8433	0.9022
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.02 (-0.62, 0.66)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9563
Hedges' G (SE)		0.01 (0.13)
Hedges' 95% CI		(-0.25, 0.27)
Hedges' P-value		0.9562

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	35	40
Mean (SD)	6.97 (3.05)	7.15 (2.85)
Week 4 (MMRM)		
n	35	39
LS mean (SE)	6.45 (0.36)	6.42 (0.34)
95% CI of LS mean	(5.73, 7.17)	(5.73, 7.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-1.03, 0.96)
Absolute Change at Week 4 (MMRM)		
n	33	38
LS mean (SE)	-0.50 (0.46)	-0.80 (0.43)
95% CI of LS mean	(-1.42, 0.42)	(-1.66, 0.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-1.56, 0.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 24 (MMRM)		
n	33	33
LS mean (SE)	6.20 (0.34)	6.54 (0.33)
95% CI of LS mean	(5.52, 6.88)	(5.88, 7.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.34 (-0.62, 1.30)
Absolute Change at Week 24 (MMRM)		
n	31	32
LS mean (SE)	-0.69 (0.44)	-0.59 (0.42)
95% CI of LS mean	(-1.57, 0.19)	(-1.43, 0.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-1.13, 1.32)
Week 52		
n	35	36
Mean (SD)	6.23 (1.75)	6.17 (1.98)
Absolute Change at Week 52		
n	33	35
Mean (SD)	-0.64 (3.10)	-0.63 (2.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52 (MMRM)		
n	33	36
LS mean (SE)	6.34 (0.32)	6.24 (0.31)
95% CI of LS mean	(5.70, 6.99)	(5.62, 6.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-1.00, 0.79)
Absolute Change at Week 52 (MMRM)		
n	31	35
LS mean (SE)	-0.51 (0.57)	-0.84 (0.53)
95% CI of LS mean	(-1.65, 0.62)	(-1.90, 0.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.32 (-1.88, 1.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change through Week 52 (MMRM)		
n	32	35
LS mean (SE)	-0.60 (0.47)	-0.72 (0.44)
95% CI of LS mean	(-1.53, 0.33)	(-1.59, 0.16)
P-value within Treatment	0.2012	0.1066
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-1.40, 1.17)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8588
Hedges' G (SE)		-0.04 (0.24)
Hedges' 95% CI		(-0.53, 0.44)
Hedges' P-value		0.8580

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	243	240
Mean (SD)	6.94 (2.87)	6.94 (2.82)
Week 4 (MMRM)		
n	240	230
LS mean (SE)	7.05 (0.19)	6.89 (0.19)
95% CI of LS mean	(6.68, 7.42)	(6.51, 7.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-0.69, 0.36)
Absolute Change at Week 4 (MMRM)		
n	233	229
LS mean (SE)	0.08 (0.14)	-0.10 (0.14)
95% CI of LS mean	(-0.19, 0.35)	(-0.37, 0.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-0.56, 0.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 24 (MMRM)		
n	236	227
LS mean (SE)	7.02 (0.20)	7.17 (0.21)
95% CI of LS mean	(6.62, 7.41)	(6.77, 7.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-0.41, 0.72)
Absolute Change at Week 24 (MMRM)		
n	229	224
LS mean (SE)	0.01 (0.18)	0.17 (0.18)
95% CI of LS mean	(-0.33, 0.36)	(-0.18, 0.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-0.34, 0.64)
Week 52		
n	239	223
Mean (SD)	7.02 (3.12)	6.87 (2.95)
Absolute Change at Week 52		
n	231	220
Mean (SD)	0.01 (2.79)	-0.05 (2.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52 (MMRM)		
n	232	217
LS mean (SE)	7.02 (0.20)	6.94 (0.20)
95% CI of LS mean	(6.63, 7.41)	(6.54, 7.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-0.64, 0.47)
Absolute Change at Week 52 (MMRM)		
n	225	214
LS mean (SE)	0.03 (0.18)	-0.06 (0.18)
95% CI of LS mean	(-0.32, 0.37)	(-0.41, 0.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.58, 0.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change through Week 52 (MMRM)		
n	233	226
LS mean (SE)	0.02 (0.16)	0.05 (0.16)
95% CI of LS mean	(-0.28, 0.33)	(-0.26, 0.36)
P-value within Treatment	0.8920	0.7351
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.03 (-0.40, 0.47)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8841
Hedges' G (SE)		0.01 (0.09)
Hedges' 95% CI		(-0.17, 0.20)
Hedges' P-value		0.8840

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	78	71
Mean (SD)	7.08 (2.68)	6.87 (3.37)
Week 4 (MMRM)		
n	78	67
LS mean (SE)	7.25 (0.37)	6.99 (0.40)
95% CI of LS mean	(6.52, 7.98)	(6.20, 7.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.27 (-1.34, 0.81)
Absolute Change at Week 4 (MMRM)		
n	76	66
LS mean (SE)	0.15 (0.27)	0.02 (0.29)
95% CI of LS mean	(-0.39, 0.70)	(-0.56, 0.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-0.93, 0.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 24 (MMRM)		
n	75	62
LS mean (SE)	7.49 (0.36)	6.87 (0.39)
95% CI of LS mean	(6.77, 8.20)	(6.09, 7.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.62 (-1.67, 0.44)
Absolute Change at Week 24 (MMRM)		
n	73	61
LS mean (SE)	0.38 (0.32)	-0.05 (0.35)
95% CI of LS mean	(-0.25, 1.01)	(-0.74, 0.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.43 (-1.37, 0.50)
Week 52		
n	78	64
Mean (SD)	7.15 (3.42)	6.53 (2.76)
Absolute Change at Week 52		
n	76	63
Mean (SD)	0.08 (2.33)	0.03 (2.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52 (MMRM)		
n	77	61
LS mean (SE)	7.21 (0.36)	6.69 (0.40)
95% CI of LS mean	(6.50, 7.92)	(5.91, 7.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.52 (-1.58, 0.54)
Absolute Change at Week 52 (MMRM)		
n	75	60
LS mean (SE)	0.12 (0.28)	-0.08 (0.32)
95% CI of LS mean	(-0.44, 0.68)	(-0.71, 0.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.20 (-1.05, 0.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change through Week 52 (MMRM)		
n	76	63
LS mean (SE)	0.25 (0.26)	-0.07 (0.29)
95% CI of LS mean	(-0.27, 0.77)	(-0.63, 0.50)
P-value within Treatment	0.3386	0.8116
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.32 (-1.09, 0.45)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4126
Hedges' G (SE)		-0.14 (0.17)
Hedges' 95% CI		(-0.48, 0.20)
Hedges' P-value		0.4121

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	194	207
Mean (SD)	6.91 (3.01)	7.01 (2.63)
Week 4 (MMRM)		
n	197	202
LS mean (SE)	6.86 (0.19)	6.77 (0.18)
95% CI of LS mean	(6.49, 7.23)	(6.41, 7.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.61, 0.42)
Absolute Change at Week 4 (MMRM)		
n	190	201
LS mean (SE)	-0.05 (0.15)	-0.27 (0.15)
95% CI of LS mean	(-0.35, 0.24)	(-0.55, 0.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-0.62, 0.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 24 (MMRM)		
n	194	198
LS mean (SE)	6.68 (0.21)	7.15 (0.21)
95% CI of LS mean	(6.27, 7.09)	(6.74, 7.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.47 (-0.10, 1.05)
Absolute Change at Week 24 (MMRM)		
n	187	195
LS mean (SE)	-0.26 (0.19)	0.09 (0.18)
95% CI of LS mean	(-0.64, 0.11)	(-0.27, 0.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-0.16, 0.88)
Week 52		
n	190	193
Mean (SD)	6.79 (2.73)	6.84 (2.86)
Absolute Change at Week 52		
n	183	190
Mean (SD)	-0.14 (3.06)	-0.22 (2.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52 (MMRM)		
n	188	192
LS mean (SE)	6.82 (0.20)	6.90 (0.20)
95% CI of LS mean	(6.42, 7.22)	(6.50, 7.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-0.49, 0.64)
Absolute Change at Week 52 (MMRM)		
n	181	189
LS mean (SE)	-0.11 (0.21)	-0.16 (0.20)
95% CI of LS mean	(-0.52, 0.29)	(-0.56, 0.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-0.61, 0.52)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change through Week 52 (MMRM)		
n	189	198
LS mean (SE)	-0.19 (0.18)	-0.03 (0.17)
95% CI of LS mean	(-0.54, 0.16)	(-0.38, 0.31)
P-value within Treatment	0.2883	0.8436
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-0.33, 0.64)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5339
Hedges' G (SE)		0.06 (0.10)
Hedges' 95% CI		(-0.14, 0.26)
Hedges' P-value		0.5338

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	139	147
Mean (SD)	6.66 (2.34)	6.61 (2.48)
Week 4 (MMRM)		
n	133	140
LS mean (SE)	6.56 (0.21)	6.55 (0.20)
95% CI of LS mean	(6.15, 6.97)	(6.15, 6.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.01 (-0.58, 0.57)
Absolute Change at Week 4 (MMRM)		
n	130	139
LS mean (SE)	-0.14 (0.17)	-0.17 (0.16)
95% CI of LS mean	(-0.47, 0.18)	(-0.48, 0.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.02 (-0.48, 0.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 24 (MMRM)		
n	131	138
LS mean (SE)	6.59 (0.24)	6.67 (0.23)
95% CI of LS mean	(6.11, 7.06)	(6.22, 7.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.09 (-0.57, 0.75)
Absolute Change at Week 24 (MMRM)		
n	128	136
LS mean (SE)	-0.12 (0.19)	-0.05 (0.18)
95% CI of LS mean	(-0.49, 0.24)	(-0.41, 0.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-0.44, 0.58)
Week 52		
n	138	140
Mean (SD)	6.66 (2.83)	6.31 (2.60)
Absolute Change at Week 52		
n	134	138
Mean (SD)	-0.04 (2.58)	-0.28 (1.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52 (MMRM)		
n	130	136
LS mean (SE)	6.63 (0.24)	6.38 (0.23)
95% CI of LS mean	(6.17, 7.10)	(5.93, 6.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-0.90, 0.40)
Absolute Change at Week 52 (MMRM)		
n	127	134
LS mean (SE)	-0.04 (0.21)	-0.34 (0.20)
95% CI of LS mean	(-0.44, 0.37)	(-0.73, 0.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-0.86, 0.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change through Week 52 (MMRM)		
n	130	138
LS mean (SE)	-0.08 (0.17)	-0.19 (0.16)
95% CI of LS mean	(-0.41, 0.25)	(-0.51, 0.13)
P-value within Treatment	0.6326	0.2340
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-0.58, 0.35)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6288
Hedges' G (SE)		-0.06 (0.12)
Hedges' 95% CI		(-0.30, 0.18)
Hedges' P-value		0.6267

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	139	133
Mean (SD)	7.23 (3.34)	7.37 (3.12)
Week 4 (MMRM)		
n	142	129
LS mean (SE)	7.32 (0.27)	7.18 (0.28)
95% CI of LS mean	(6.79, 7.84)	(6.63, 7.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-0.90, 0.63)
Absolute Change at Week 4 (MMRM)		
n	136	128
LS mean (SE)	0.15 (0.21)	-0.22 (0.21)
95% CI of LS mean	(-0.26, 0.55)	(-0.64, 0.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.37 (-0.96, 0.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 24 (MMRM)		
n	138	122
LS mean (SE)	7.15 (0.27)	7.56 (0.29)
95% CI of LS mean	(6.62, 7.68)	(7.00, 8.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.41 (-0.37, 1.19)
Absolute Change at Week 24 (MMRM)		
n	132	120
LS mean (SE)	-0.05 (0.27)	0.18 (0.28)
95% CI of LS mean	(-0.58, 0.48)	(-0.37, 0.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.23 (-0.54, 1.01)
Week 52		
n	136	119
Mean (SD)	7.18 (3.13)	7.32 (3.03)
Absolute Change at Week 52		
n	130	117
Mean (SD)	-0.10 (3.08)	0.04 (2.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52 (MMRM)		
n	135	117
LS mean (SE)	7.16 (0.26)	7.43 (0.28)
95% CI of LS mean	(6.64, 7.69)	(6.88, 7.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.27 (-0.50, 1.03)
Absolute Change at Week 52 (MMRM)		
n	129	115
LS mean (SE)	-0.05 (0.27)	0.07 (0.28)
95% CI of LS mean	(-0.59, 0.48)	(-0.49, 0.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-0.65, 0.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change through Week 52 (MMRM)		
n	135	123
LS mean (SE)	-0.05 (0.25)	0.13 (0.26)
95% CI of LS mean	(-0.54, 0.43)	(-0.38, 0.63)
P-value within Treatment	0.8308	0.6272
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-0.53, 0.88)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6192
Hedges' G (SE)		0.06 (0.12)
Hedges' 95% CI		(-0.18, 0.31)
Hedges' P-value		0.6181

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	99	112
Mean (SD)	7.00 (2.86)	6.72 (2.47)
Week 4 (MMRM)		
n	98	110
LS mean (SE)	7.29 (0.27)	6.65 (0.25)
95% CI of LS mean	(6.76, 7.82)	(6.15, 7.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-1.37, 0.09)
Absolute Change at Week 4 (MMRM)		
n	94	108
LS mean (SE)	0.23 (0.19)	-0.11 (0.17)
95% CI of LS mean	(-0.14, 0.60)	(-0.45, 0.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.34 (-0.85, 0.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 24 (MMRM)		
n	97	106
LS mean (SE)	7.33 (0.29)	6.61 (0.28)
95% CI of LS mean	(6.75, 7.91)	(6.07, 7.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.71 (-1.51, 0.08)
Absolute Change at Week 24 (MMRM)		
n	93	104
LS mean (SE)	0.30 (0.23)	-0.09 (0.22)
95% CI of LS mean	(-0.16, 0.76)	(-0.53, 0.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.39 (-1.03, 0.24)
Week 52		
n	97	102
Mean (SD)	7.09 (2.61)	6.25 (1.83)
Absolute Change at Week 52		
n	93	100
Mean (SD)	0.08 (2.29)	-0.32 (1.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52 (MMRM)		
n	93	102
LS mean (SE)	7.12 (0.23)	6.33 (0.22)
95% CI of LS mean	(6.66, 7.58)	(5.90, 6.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.79 (-1.42, -0.15)
Absolute Change at Week 52 (MMRM)		
n	89	100
LS mean (SE)	0.08 (0.23)	-0.33 (0.22)
95% CI of LS mean	(-0.37, 0.53)	(-0.76, 0.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.41 (-1.04, 0.21)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change through Week 52 (MMRM)		
n	94	105
LS mean (SE)	0.19 (0.20)	-0.21 (0.19)
95% CI of LS mean	(-0.21, 0.59)	(-0.59, 0.16)
P-value within Treatment	0.3460	0.2600
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.40 (-0.95, 0.14)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1461
Hedges' G (SE)		-0.21 (0.14)
Hedges' 95% CI		(-0.49, 0.07)
Hedges' P-value		0.1462

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	179	168
Mean (SD)	6.92 (2.91)	7.14 (3.03)
Week 4 (MMRM)		
n	177	159
LS mean (SE)	6.80 (0.22)	6.94 (0.23)
95% CI of LS mean	(6.37, 7.23)	(6.49, 7.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-0.48, 0.76)
Absolute Change at Week 4 (MMRM)		
n	172	159
LS mean (SE)	-0.12 (0.18)	-0.25 (0.19)
95% CI of LS mean	(-0.47, 0.23)	(-0.62, 0.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-0.64, 0.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 24 (MMRM)		
n	172	154
LS mean (SE)	6.66 (0.23)	7.39 (0.24)
95% CI of LS mean	(6.21, 7.11)	(6.92, 7.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.73 (0.07, 1.39)
Absolute Change at Week 24 (MMRM)		
n	167	152
LS mean (SE)	-0.30 (0.22)	0.18 (0.23)
95% CI of LS mean	(-0.73, 0.13)	(-0.27, 0.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.47 (-0.15, 1.10)
Week 52		
n	177	157
Mean (SD)	6.82 (3.19)	7.11 (3.30)
Absolute Change at Week 52		
n	171	155
Mean (SD)	-0.15 (3.09)	-0.01 (2.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52 (MMRM)		
n	172	151
LS mean (SE)	6.83 (0.24)	7.18 (0.26)
95% CI of LS mean	(6.35, 7.31)	(6.67, 7.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.35 (-0.35, 1.05)
Absolute Change at Week 52 (MMRM)		
n	167	149
LS mean (SE)	-0.12 (0.23)	-0.04 (0.24)
95% CI of LS mean	(-0.57, 0.33)	(-0.52, 0.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-0.58, 0.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Emotional
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	171	156
LS mean (SE)	-0.21 (0.20)	0.07 (0.21)
95% CI of LS mean	(-0.61, 0.19)	(-0.35, 0.48)
P-value within Treatment	0.3033	0.7504
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.28 (-0.30, 0.85)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3474
Hedges' G (SE)		0.10 (0.11)
Hedges' 95% CI		(-0.11, 0.32)
Hedges' P-value		0.3472

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	159	152
Mean (SD)	5.49 (2.30)	5.20 (2.20)
Week 4 (MMRM)		
n	158	146
LS mean (SE)	5.45 (0.18)	5.16 (0.18)
95% CI of LS mean	(5.11, 5.80)	(4.81, 5.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.29 (-0.79, 0.21)
Absolute Change at Week 4 (MMRM)		
n	151	145
LS mean (SE)	-0.02 (0.14)	-0.07 (0.14)
95% CI of LS mean	(-0.29, 0.25)	(-0.35, 0.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-0.44, 0.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 24 (MMRM)		
n	154	143
LS mean (SE)	5.62 (0.19)	5.27 (0.20)
95% CI of LS mean	(5.25, 5.99)	(4.89, 5.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.34 (-0.88, 0.19)
Absolute Change at Week 24 (MMRM)		
n	147	142
LS mean (SE)	0.11 (0.15)	0.03 (0.15)
95% CI of LS mean	(-0.18, 0.40)	(-0.26, 0.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-0.49, 0.33)
Week 52		
n	155	140
Mean (SD)	5.45 (2.44)	4.82 (1.95)
Absolute Change at Week 52		
n	148	138
Mean (SD)	-0.09 (1.70)	-0.28 (1.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52 (MMRM)		
n	150	139
LS mean (SE)	5.39 (0.18)	4.93 (0.18)
95% CI of LS mean	(5.04, 5.74)	(4.57, 5.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.46 (-0.96, 0.04)
Absolute Change at Week 52 (MMRM)		
n	143	137
LS mean (SE)	-0.12 (0.14)	-0.29 (0.14)
95% CI of LS mean	(-0.39, 0.16)	(-0.57, -0.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-0.57, 0.21)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change through Week 52 (MMRM)		
n	150	143
LS mean (SE)	0.00 (0.12)	-0.13 (0.12)
95% CI of LS mean	(-0.24, 0.23)	(-0.37, 0.11)
P-value within Treatment	0.9796	0.2887
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-0.47, 0.21)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4599
Hedges' G (SE)		-0.09 (0.12)
Hedges' 95% CI		(-0.32, 0.14)
Hedges' P-value		0.4597

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	114	124
Mean (SD)	4.85 (2.01)	5.05 (1.95)
Week 4 (MMRM)		
n	115	119
LS mean (SE)	4.89 (0.19)	4.87 (0.19)
95% CI of LS mean	(4.51, 5.28)	(4.49, 5.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.02 (-0.56, 0.52)
Absolute Change at Week 4 (MMRM)		
n	110	118
LS mean (SE)	-0.01 (0.14)	-0.13 (0.14)
95% CI of LS mean	(-0.28, 0.27)	(-0.40, 0.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-0.52, 0.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 24 (MMRM)		
n	113	113
LS mean (SE)	4.87 (0.19)	4.79 (0.19)
95% CI of LS mean	(4.50, 5.24)	(4.42, 5.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-0.60, 0.44)
Absolute Change at Week 24 (MMRM)		
n	108	112
LS mean (SE)	0.01 (0.16)	-0.21 (0.15)
95% CI of LS mean	(-0.30, 0.32)	(-0.52, 0.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-0.66, 0.21)
Week 52		
n	115	114
Mean (SD)	4.60 (1.98)	4.52 (1.84)
Absolute Change at Week 52		
n	110	113
Mean (SD)	-0.25 (1.88)	-0.44 (1.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52 (MMRM)		
n	114	113
LS mean (SE)	4.59 (0.18)	4.56 (0.18)
95% CI of LS mean	(4.24, 4.94)	(4.21, 4.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-0.53, 0.48)
Absolute Change at Week 52 (MMRM)		
n	109	112
LS mean (SE)	-0.23 (0.17)	-0.44 (0.16)
95% CI of LS mean	(-0.56, 0.10)	(-0.76, -0.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.21 (-0.66, 0.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change through Week 52 (MMRM)		
n	112	118
LS mean (SE)	-0.11 (0.14)	-0.33 (0.14)
95% CI of LS mean	(-0.39, 0.17)	(-0.60, -0.05)
P-value within Treatment	0.4417	0.0188
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-0.61, 0.17)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2731
Hedges' G (SE)		-0.14 (0.13)
Hedges' 95% CI		(-0.40, 0.11)
Hedges' P-value		0.2725

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	34	40
Mean (SD)	4.47 (1.86)	5.03 (2.08)
Week 4 (MMRM)		
n	35	38
LS mean (SE)	4.27 (0.25)	4.34 (0.24)
95% CI of LS mean	(3.77, 4.77)	(3.86, 4.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-0.63, 0.76)
Absolute Change at Week 4 (MMRM)		
n	32	37
LS mean (SE)	-0.32 (0.20)	-0.50 (0.18)
95% CI of LS mean	(-0.72, 0.07)	(-0.86, -0.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-0.72, 0.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 24 (MMRM)		
n	33	32
LS mean (SE)	3.94 (0.21)	4.04 (0.21)
95% CI of LS mean	(3.52, 4.37)	(3.62, 4.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-0.51, 0.70)
Absolute Change at Week 24 (MMRM)		
n	30	31
LS mean (SE)	-0.57 (0.29)	-0.76 (0.28)
95% CI of LS mean	(-1.15, 0.01)	(-1.31, -0.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.19 (-1.00, 0.61)
Week 52		
n	35	36
Mean (SD)	4.06 (1.59)	4.03 (1.72)
Absolute Change at Week 52		
n	32	35
Mean (SD)	-0.34 (1.75)	-0.83 (1.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52 (MMRM)		
n	33	36
LS mean (SE)	4.01 (0.29)	4.08 (0.28)
95% CI of LS mean	(3.43, 4.59)	(3.53, 4.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-0.74, 0.88)
Absolute Change at Week 52 (MMRM)		
n	30	35
LS mean (SE)	-0.44 (0.33)	-0.81 (0.30)
95% CI of LS mean	(-1.09, 0.22)	(-1.42, -0.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-1.27, 0.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change through Week 52 (MMRM)		
n	31	35
LS mean (SE)	-0.50 (0.28)	-0.79 (0.26)
95% CI of LS mean	(-1.06, 0.06)	(-1.31, -0.26)
P-value within Treatment	0.0785	0.0038
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.29 (-1.06, 0.48)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4612
Hedges' G (SE)		-0.18 (0.24)
Hedges' 95% CI		(-0.67, 0.31)
Hedges' P-value		0.4605

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	242	241
Mean (SD)	5.32 (2.22)	5.15 (2.07)
Week 4 (MMRM)		
n	238	227
LS mean (SE)	5.36 (0.15)	5.14 (0.15)
95% CI of LS mean	(5.07, 5.64)	(4.85, 5.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-0.63, 0.19)
Absolute Change at Week 4 (MMRM)		
n	229	226
LS mean (SE)	0.02 (0.11)	-0.03 (0.11)
95% CI of LS mean	(-0.20, 0.24)	(-0.24, 0.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-0.35, 0.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 24 (MMRM)		
n	234	224
LS mean (SE)	5.50 (0.15)	5.21 (0.15)
95% CI of LS mean	(5.20, 5.80)	(4.91, 5.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.28 (-0.71, 0.14)
Absolute Change at Week 24 (MMRM)		
n	225	223
LS mean (SE)	0.14 (0.12)	0.03 (0.12)
95% CI of LS mean	(-0.08, 0.37)	(-0.20, 0.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-0.44, 0.21)
Week 52		
n	238	222
Mean (SD)	5.24 (2.33)	4.80 (1.92)
Absolute Change at Week 52		
n	229	220
Mean (SD)	-0.13 (1.77)	-0.27 (1.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52 (MMRM)		
n	231	216
LS mean (SE)	5.21 (0.14)	4.87 (0.14)
95% CI of LS mean	(4.93, 5.48)	(4.59, 5.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-0.73, 0.06)
Absolute Change at Week 52 (MMRM)		
n	222	214
LS mean (SE)	-0.14 (0.11)	-0.28 (0.11)
95% CI of LS mean	(-0.36, 0.08)	(-0.50, -0.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-0.46, 0.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change through Week 52 (MMRM)		
n	231	226
LS mean (SE)	0.00 (0.10)	-0.12 (0.10)
95% CI of LS mean	(-0.19, 0.20)	(-0.32, 0.07)
P-value within Treatment	0.9664	0.2057
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-0.40, 0.14)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3534
Hedges' G (SE)		-0.09 (0.09)
Hedges' 95% CI		(-0.27, 0.10)
Hedges' P-value		0.3530

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	77	71
Mean (SD)	5.57 (2.58)	4.92 (2.12)
Week 4 (MMRM)		
n	77	67
LS mean (SE)	5.57 (0.25)	4.76 (0.27)
95% CI of LS mean	(5.09, 6.06)	(4.23, 5.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.82 (-1.53, -0.10)
Absolute Change at Week 4 (MMRM)		
n	74	66
LS mean (SE)	-0.06 (0.18)	-0.12 (0.20)
95% CI of LS mean	(-0.43, 0.30)	(-0.50, 0.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-0.59, 0.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 24 (MMRM)		
n	76	60
LS mean (SE)	6.02 (0.26)	4.75 (0.29)
95% CI of LS mean	(5.50, 6.54)	(4.18, 5.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.26 (-2.04, -0.49)
Absolute Change at Week 24 (MMRM)		
n	73	59
LS mean (SE)	0.42 (0.21)	-0.13 (0.24)
95% CI of LS mean	(0.00, 0.84)	(-0.60, 0.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.55 (-1.18, 0.08)
Week 52		
n	78	63
Mean (SD)	5.32 (2.35)	4.49 (1.77)
Absolute Change at Week 52		
n	75	62
Mean (SD)	-0.25 (1.82)	-0.16 (1.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52 (MMRM)		
n	77	60
LS mean (SE)	5.32 (0.23)	4.56 (0.25)
95% CI of LS mean	(4.87, 5.77)	(4.06, 5.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.76 (-1.44, -0.08)
Absolute Change at Week 52 (MMRM)		
n	74	59
LS mean (SE)	-0.23 (0.21)	-0.27 (0.23)
95% CI of LS mean	(-0.64, 0.18)	(-0.73, 0.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-0.65, 0.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change through Week 52 (MMRM)		
n	75	62
LS mean (SE)	0.09 (0.18)	-0.20 (0.20)
95% CI of LS mean	(-0.27, 0.45)	(-0.60, 0.19)
P-value within Treatment	0.6056	0.3091
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-0.83, 0.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2732
Hedges' G (SE)		-0.19 (0.17)
Hedges' 95% CI		(-0.53, 0.15)
Hedges' P-value		0.2726

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	192	208
Mean (SD)	5.08 (2.02)	5.22 (2.06)
Week 4 (MMRM)		
n	196	198
LS mean (SE)	5.08 (0.15)	5.12 (0.15)
95% CI of LS mean	(4.77, 5.38)	(4.82, 5.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.04 (-0.39, 0.46)
Absolute Change at Week 4 (MMRM)		
n	187	197
LS mean (SE)	0.00 (0.12)	-0.08 (0.11)
95% CI of LS mean	(-0.23, 0.23)	(-0.31, 0.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-0.40, 0.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 24 (MMRM)		
n	191	196
LS mean (SE)	5.02 (0.15)	5.15 (0.15)
95% CI of LS mean	(4.72, 5.32)	(4.85, 5.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-0.29, 0.56)
Absolute Change at Week 24 (MMRM)		
n	182	195
LS mean (SE)	-0.08 (0.12)	-0.06 (0.12)
95% CI of LS mean	(-0.32, 0.16)	(-0.29, 0.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.02 (-0.32, 0.35)
Week 52		
n	189	193
Mean (SD)	4.99 (2.25)	4.77 (1.95)
Absolute Change at Week 52		
n	180	191
Mean (SD)	-0.12 (1.77)	-0.41 (1.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52 (MMRM)		
n	187	192
LS mean (SE)	4.95 (0.15)	4.82 (0.15)
95% CI of LS mean	(4.65, 5.25)	(4.53, 5.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-0.55, 0.29)
Absolute Change at Week 52 (MMRM)		
n	178	190
LS mean (SE)	-0.14 (0.12)	-0.38 (0.12)
95% CI of LS mean	(-0.39, 0.10)	(-0.62, -0.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-0.58, 0.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change through Week 52 (MMRM)		
n	187	199
LS mean (SE)	-0.11 (0.11)	-0.22 (0.10)
95% CI of LS mean	(-0.32, 0.10)	(-0.42, -0.02)
P-value within Treatment	0.2992	0.0312
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-0.40, 0.18)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4501
Hedges' G (SE)		-0.08 (0.10)
Hedges' 95% CI		(-0.28, 0.12)
Hedges' P-value		0.4500

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	138	147
Mean (SD)	4.90 (2.04)	4.81 (2.00)
Week 4 (MMRM)		
n	132	140
LS mean (SE)	4.90 (0.18)	4.86 (0.18)
95% CI of LS mean	(4.55, 5.26)	(4.51, 5.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-0.55, 0.46)
Absolute Change at Week 4 (MMRM)		
n	127	138
LS mean (SE)	-0.05 (0.14)	0.07 (0.13)
95% CI of LS mean	(-0.33, 0.22)	(-0.19, 0.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-0.25, 0.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 24 (MMRM)		
n	130	138
LS mean (SE)	5.02 (0.18)	4.71 (0.17)
95% CI of LS mean	(4.67, 5.37)	(4.37, 5.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-0.80, 0.17)
Absolute Change at Week 24 (MMRM)		
n	125	137
LS mean (SE)	0.10 (0.14)	-0.11 (0.14)
95% CI of LS mean	(-0.19, 0.39)	(-0.38, 0.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.20 (-0.60, 0.19)
Week 52		
n	137	140
Mean (SD)	4.84 (2.25)	4.56 (1.98)
Absolute Change at Week 52		
n	132	138
Mean (SD)	-0.07 (1.74)	-0.20 (1.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52 (MMRM)		
n	129	136
LS mean (SE)	4.83 (0.18)	4.57 (0.18)
95% CI of LS mean	(4.48, 5.19)	(4.23, 4.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-0.76, 0.24)
Absolute Change at Week 52 (MMRM)		
n	124	134
LS mean (SE)	-0.08 (0.15)	-0.24 (0.14)
95% CI of LS mean	(-0.38, 0.21)	(-0.52, 0.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-0.56, 0.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change through Week 52 (MMRM)		
n	128	138
LS mean (SE)	0.01 (0.13)	-0.17 (0.12)
95% CI of LS mean	(-0.24, 0.26)	(-0.41, 0.07)
P-value within Treatment	0.9517	0.1660
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-0.53, 0.17)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3183
Hedges' G (SE)		-0.12 (0.12)
Hedges' 95% CI		(-0.36, 0.12)
Hedges' P-value		0.3159

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	138	134
Mean (SD)	5.53 (2.31)	5.49 (2.09)
Week 4 (MMRM)		
n	141	125
LS mean (SE)	5.49 (0.19)	5.24 (0.20)
95% CI of LS mean	(5.12, 5.86)	(4.85, 5.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-0.80, 0.29)
Absolute Change at Week 4 (MMRM)		
n	134	125
LS mean (SE)	0.03 (0.14)	-0.29 (0.15)
95% CI of LS mean	(-0.25, 0.31)	(-0.57, 0.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-0.72, 0.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 24 (MMRM)		
n	137	118
LS mean (SE)	5.55 (0.20)	5.48 (0.22)
95% CI of LS mean	(5.15, 5.95)	(5.05, 5.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-0.66, 0.51)
Absolute Change at Week 24 (MMRM)		
n	130	117
LS mean (SE)	0.04 (0.16)	-0.05 (0.17)
95% CI of LS mean	(-0.28, 0.36)	(-0.38, 0.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-0.56, 0.37)
Week 52		
n	136	118
Mean (SD)	5.33 (2.30)	4.85 (1.81)
Absolute Change at Week 52		
n	129	117
Mean (SD)	-0.24 (1.80)	-0.53 (1.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52 (MMRM)		
n	135	116
LS mean (SE)	5.24 (0.18)	4.98 (0.19)
95% CI of LS mean	(4.89, 5.60)	(4.61, 5.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-0.78, 0.27)
Absolute Change at Week 52 (MMRM)		
n	128	115
LS mean (SE)	-0.24 (0.15)	-0.52 (0.16)
95% CI of LS mean	(-0.54, 0.06)	(-0.83, -0.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.28 (-0.71, 0.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change through Week 52 (MMRM)		
n	134	123
LS mean (SE)	-0.10 (0.13)	-0.28 (0.14)
95% CI of LS mean	(-0.36, 0.17)	(-0.56, -0.01)
P-value within Treatment	0.4719	0.0452
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.19 (-0.57, 0.20)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3428
Hedges' G (SE)		-0.12 (0.12)
Hedges' 95% CI		(-0.36, 0.13)
Hedges' P-value		0.3411

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	98	112
Mean (SD)	5.29 (2.35)	4.99 (2.02)
Week 4 (MMRM)		
n	98	109
LS mean (SE)	5.48 (0.22)	4.70 (0.21)
95% CI of LS mean	(5.05, 5.91)	(4.29, 5.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.79 (-1.38, -0.19)
Absolute Change at Week 4 (MMRM)		
n	93	107
LS mean (SE)	0.16 (0.14)	-0.25 (0.13)
95% CI of LS mean	(-0.12, 0.45)	(-0.51, 0.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.41 (-0.80, -0.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 24 (MMRM)		
n	97	106
LS mean (SE)	5.33 (0.21)	4.68 (0.20)
95% CI of LS mean	(4.92, 5.74)	(4.29, 5.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.65 (-1.22, -0.08)
Absolute Change at Week 24 (MMRM)		
n	92	105
LS mean (SE)	0.06 (0.16)	-0.30 (0.15)
95% CI of LS mean	(-0.25, 0.37)	(-0.58, -0.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.36 (-0.78, 0.06)
Week 52		
n	97	102
Mean (SD)	5.15 (2.25)	4.47 (1.72)
Absolute Change at Week 52		
n	92	100
Mean (SD)	-0.11 (1.39)	-0.52 (1.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52 (MMRM)		
n	93	102
LS mean (SE)	5.13 (0.20)	4.49 (0.19)
95% CI of LS mean	(4.74, 5.52)	(4.12, 4.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-1.18, -0.11)
Absolute Change at Week 52 (MMRM)		
n	88	100
LS mean (SE)	-0.12 (0.16)	-0.49 (0.15)
95% CI of LS mean	(-0.43, 0.20)	(-0.79, -0.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-0.81, 0.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change through Week 52 (MMRM)		
n	93	105
LS mean (SE)	-0.03 (0.14)	-0.40 (0.13)
95% CI of LS mean	(-0.31, 0.25)	(-0.66, -0.14)
P-value within Treatment	0.8341	0.0029
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.37 (-0.75, 0.01)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0587
Hedges' G (SE)		-0.27 (0.14)
Hedges' 95% CI		(-0.55, 0.01)
Hedges' P-value		0.0593

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	178	169
Mean (SD)	5.17 (2.12)	5.23 (2.11)
Week 4 (MMRM)		
n	175	156
LS mean (SE)	5.08 (0.16)	5.25 (0.17)
95% CI of LS mean	(4.76, 5.40)	(4.91, 5.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-0.30, 0.63)
Absolute Change at Week 4 (MMRM)		
n	168	156
LS mean (SE)	-0.13 (0.13)	0.03 (0.14)
95% CI of LS mean	(-0.39, 0.13)	(-0.24, 0.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-0.21, 0.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 24 (MMRM)		
n	170	150
LS mean (SE)	5.30 (0.18)	5.31 (0.19)
95% CI of LS mean	(4.96, 5.65)	(4.94, 5.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-0.50, 0.51)
Absolute Change at Week 24 (MMRM)		
n	163	149
LS mean (SE)	0.06 (0.14)	0.09 (0.15)
95% CI of LS mean	(-0.23, 0.34)	(-0.20, 0.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.04 (-0.37, 0.45)
Week 52		
n	176	156
Mean (SD)	5.05 (2.30)	4.83 (2.01)
Absolute Change at Week 52		
n	169	155
Mean (SD)	-0.18 (1.95)	-0.24 (1.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52 (MMRM)		
n	171	150
LS mean (SE)	5.02 (0.17)	4.94 (0.18)
95% CI of LS mean	(4.70, 5.35)	(4.59, 5.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-0.56, 0.39)
Absolute Change at Week 52 (MMRM)		
n	164	149
LS mean (SE)	-0.21 (0.14)	-0.25 (0.15)
95% CI of LS mean	(-0.49, 0.07)	(-0.54, 0.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-0.44, 0.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.13.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CF-IQ Domain Score through Week 52 by Subgroups
Full Analysis Set

Domain: Work/School Limitation
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	169	156
LS mean (SE)	-0.08 (0.12)	-0.08 (0.13)
95% CI of LS mean	(-0.32, 0.16)	(-0.32, 0.17)
P-value within Treatment	0.5191	0.5422
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-0.34, 0.34)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9950
Hedges' G (SE)		0.00 (0.11)
Hedges' 95% CI		(-0.22, 0.22)
Hedges' P-value		0.9950

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with any TEAEs	271 (93.77)	274 (96.48)
Relative Risk (RR) (95% CI)		1.0289 (0.9914, 1.0678)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1327
Odds Ratio (OR) (95% CI)		1.8199 (0.8251, 4.0142)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1379
Risk Difference (RD) (95% CI)		0.0271 (-0.0081, 0.0622)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1312
Infections and infestations	208 (71.97)	199 (70.07)
Relative Risk (RR) (95% CI)		0.9736 (0.8768, 1.0810)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6160
Odds Ratio (OR) (95% CI)		0.9117 (0.6354, 1.3082)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6159
Risk Difference (RD) (95% CI)		-0.0190 (-0.0933, 0.0553)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6158

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
COVID-19	73 (25.26)	58 (20.42)
Relative Risk (RR) (95% CI)		0.8085 (0.5969, 1.0951)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1697
Odds Ratio (OR) (95% CI)		0.7594 (0.5131, 1.1238)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1687
Risk Difference (RD) (95% CI)		-0.0484 (-0.1170, 0.0202)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1671
Nasopharyngitis	60 (20.76)	57 (20.07)
Relative Risk (RR) (95% CI)		0.9667 (0.6996, 1.3359)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8375
Odds Ratio (OR) (95% CI)		0.9584 (0.6384, 1.4388)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8375

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0069 (-0.0729, 0.0591)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8375

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Upper respiratory tract infection	40 (13.84)	55 (19.37)
Relative Risk (RR) (95% CI)		1.3992 (0.9637, 2.0316)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0775
Odds Ratio (OR) (95% CI)		1.4951 (0.9580, 2.3332)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0765
Risk Difference (RD) (95% CI)		0.0553 (-0.0056, 0.1161)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0749
Influenza	16 (5.54)	33 (11.62)
Relative Risk (RR) (95% CI)		2.0988 (1.1820, 3.7268)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0114
Odds Ratio (OR) (95% CI)		2.2433 (1.2053, 4.1750)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0108

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0608 (0.0152, 0.1065)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0090

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Viral upper respiratory tract infection	17 (5.88)	20 (7.04)
Relative Risk (RR) (95% CI)		1.1972 (0.6405, 2.2377)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5728
Odds Ratio (OR) (95% CI)		1.2121 (0.6213, 2.3649)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5727
Risk Difference (RD) (95% CI)		0.0116 (-0.0287, 0.0519)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5724
Sinusitis	26 (9.00)	9 (3.17)
Relative Risk (RR) (95% CI)		0.3522 (0.1680, 0.7384)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0057
Odds Ratio (OR) (95% CI)		0.3310 (0.1523, 0.7197)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0053

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0583 (-0.0970, -0.0195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0032

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Urinary tract infection	10 (3.46)	9 (3.17)
Relative Risk (RR) (95% CI)		0.9158 (0.3778, 2.2202)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8457
Odds Ratio (OR) (95% CI)		0.9131 (0.3654, 2.2816)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8457
Risk Difference (RD) (95% CI)		-0.0029 (-0.0322, 0.0264)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8456
Rhinitis	11 (3.81)	8 (2.82)
Relative Risk (RR) (95% CI)		0.7401 (0.3021, 1.8128)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5102
Odds Ratio (OR) (95% CI)		0.7325 (0.2902, 1.8489)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5100

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0099 (-0.0392, 0.0194)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5077

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Bronchitis	8 (2.77)	7 (2.46)
Relative Risk (RR) (95% CI)		0.8904 (0.3272, 2.4230)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8202
Odds Ratio (OR) (95% CI)		0.8876 (0.3176, 2.4810)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8202
Risk Difference (RD) (95% CI)		-0.0030 (-0.0292, 0.0231)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8200
Gastroenteritis	4 (1.38)	7 (2.46)
Relative Risk (RR) (95% CI)		1.7808 (0.5271, 6.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3529
Odds Ratio (OR) (95% CI)		1.8005 (0.5213, 6.2192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3524

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0108 (-0.0117, 0.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3467

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Conjunctivitis	12 (4.15)	5 (1.76)
Relative Risk (RR) (95% CI)		0.4240 (0.1513, 1.1881)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1026
Odds Ratio (OR) (95% CI)		0.4137 (0.1438, 1.1898)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1015
Risk Difference (RD) (95% CI)		-0.0239 (-0.0515, 0.0037)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0897
Pharyngitis	8 (2.77)	5 (1.76)
Relative Risk (RR) (95% CI)		0.6360 (0.2106, 1.9208)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4223
Odds Ratio (OR) (95% CI)		0.6295 (0.2034, 1.9478)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4219

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Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0101 (-0.0344, 0.0142)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4169

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Vulvovaginal mycotic infection	7 (2.42)	5 (1.76)
Relative Risk (RR) (95% CI)		0.7269 (0.2334, 2.2634)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5820
Odds Ratio (OR) (95% CI)		0.7220 (0.2264, 2.3019)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5819
Risk Difference (RD) (95% CI)		-0.0066 (-0.0300, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5797
Otitis media	6 (2.08)	4 (1.41)
Relative Risk (RR) (95% CI)		0.6784 (0.1935, 2.3786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5444
Odds Ratio (OR) (95% CI)		0.6738 (0.1881, 2.4135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5442

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0067 (-0.0281, 0.0147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5409

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Pneumonia	8 (2.77)	4 (1.41)
Relative Risk (RR) (95% CI)		0.5088 (0.1549, 1.6708)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2654
Odds Ratio (OR) (95% CI)		0.5018 (0.1494, 1.6854)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2646
Risk Difference (RD) (95% CI)		-0.0136 (-0.0370, 0.0098)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2539
Respiratory, thoracic and mediastinal disorders	153 (52.94)	145 (51.06)
Relative Risk (RR) (95% CI)		0.9644 (0.8239, 1.1288)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6517
Odds Ratio (OR) (95% CI)		0.9273 (0.6681, 1.2870)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6516
Risk Difference (RD) (95% CI)		-0.0188 (-0.1007, 0.0630)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6516

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Cough	60 (20.76)	63 (22.18)
Relative Risk (RR) (95% CI)		1.0685 (0.7811, 1.4617)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6786
Odds Ratio (OR) (95% CI)		1.0880 (0.7301, 1.6214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6786
Risk Difference (RD) (95% CI)		0.0142 (-0.0530, 0.0815)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6786
Oropharyngeal pain	37 (12.80)	45 (15.85)
Relative Risk (RR) (95% CI)		1.2376 (0.8272, 1.8518)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2997
Odds Ratio (OR) (95% CI)		1.2824 (0.8018, 2.0509)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2992

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0304 (-0.0269, 0.0878)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2984

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Nasal congestion	23 (7.96)	29 (10.21)
Relative Risk (RR) (95% CI)		1.2831 (0.7612, 2.1629)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3495
Odds Ratio (OR) (95% CI)		1.3153 (0.7412, 2.3341)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3491
Risk Difference (RD) (95% CI)		0.0225 (-0.0245, 0.0696)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3480
Sputum increased	29 (10.03)	27 (9.51)
Relative Risk (RR) (95% CI)		0.9474 (0.5758, 1.5588)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8316
Odds Ratio (OR) (95% CI)		0.9419 (0.5425, 1.6355)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8316

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0053 (-0.0539, 0.0433)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8316

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Sinus congestion	10 (3.46)	18 (6.34)
Relative Risk (RR) (95% CI)		1.8317 (0.8605, 3.8990)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1164
Odds Ratio (OR) (95% CI)		1.8880 (0.8559, 4.1643)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1154
Risk Difference (RD) (95% CI)		0.0288 (-0.0065, 0.0641)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1102
Haemoptysis	22 (7.61)	17 (5.99)
Relative Risk (RR) (95% CI)		0.7863 (0.4267, 1.4492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4409
Odds Ratio (OR) (95% CI)		0.7727 (0.4013, 1.4880)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4406

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0163 (-0.0574, 0.0249)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4389

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Productive cough	19 (6.57)	16 (5.63)
Relative Risk (RR) (95% CI)		0.8569 (0.4498, 1.6326)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6387
Odds Ratio (OR) (95% CI)		0.8484 (0.4272, 1.6850)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6386
Risk Difference (RD) (95% CI)		-0.0094 (-0.0486, 0.0298)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6380
Rhinorrhoea	22 (7.61)	16 (5.63)
Relative Risk (RR) (95% CI)		0.7401 (0.3970, 1.3796)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3435
Odds Ratio (OR) (95% CI)		0.7246 (0.3723, 1.4102)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3430

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0198 (-0.0605, 0.0209)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3403

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Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Dyspnoea	21 (7.27)	11 (3.87)
Relative Risk (RR) (95% CI)		0.5330 (0.2618, 1.0851)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0828
Odds Ratio (OR) (95% CI)		0.5142 (0.2432, 1.0872)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0817
Risk Difference (RD) (95% CI)		-0.0339 (-0.0713, 0.0035)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0754
Lower respiratory tract congestion	5 (1.73)	9 (3.17)
Relative Risk (RR) (95% CI)		1.8317 (0.6215, 5.3985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2724
Odds Ratio (OR) (95% CI)		1.8589 (0.6152, 5.6165)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2718

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Study VX20-121-103: Summary of TEAEs by SOC and PT
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Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0144 (-0.0109, 0.0397)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2653

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Study VX20-121-103: Summary of TEAEs by SOC and PT
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Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Respiration abnormal	7 (2.42)	9 (3.17)
Relative Risk (RR) (95% CI)		1.3084 (0.4940, 3.4654)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5886
Odds Ratio (OR) (95% CI)		1.3184 (0.4843, 3.5896)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5885
Risk Difference (RD) (95% CI)		0.0075 (-0.0195, 0.0345)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5878
Wheezing	7 (2.42)	8 (2.82)
Relative Risk (RR) (95% CI)		1.1630 (0.4274, 3.1647)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7675
Odds Ratio (OR) (95% CI)		1.1677 (0.4178, 3.2638)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7675

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Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0039 (-0.0222, 0.0301)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7674

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Upper-airway cough syndrome	8 (2.77)	2 (0.70)
Relative Risk (RR) (95% CI)		0.2544 (0.0545, 1.1876)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0816
Odds Ratio (OR) (95% CI)		0.2491 (0.0524, 1.1834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0804
Risk Difference (RD) (95% CI)		-0.0206 (-0.0419, 0.0006)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0572
Gastrointestinal disorders	111 (38.41)	114 (40.14)
Relative Risk (RR) (95% CI)		1.0451 (0.8525, 1.2812)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6712
Odds Ratio (OR) (95% CI)		1.0754 (0.7689, 1.5039)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6711
Risk Difference (RD) (95% CI)		0.0173 (-0.0626, 0.0973)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6711

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(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Diarrhoea	44 (15.22)	37 (13.03)
Relative Risk (RR) (95% CI)		0.8557 (0.5705, 1.2834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4512
Odds Ratio (OR) (95% CI)		0.8341 (0.5205, 1.3366)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4509
Risk Difference (RD) (95% CI)		-0.0220 (-0.0790, 0.0350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4500
Nausea	13 (4.50)	22 (7.75)
Relative Risk (RR) (95% CI)		1.7221 (0.8849, 3.3513)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1096
Odds Ratio (OR) (95% CI)		1.7827 (0.8798, 3.6122)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1086

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0325 (-0.0067, 0.0717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1045

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Abdominal pain	23 (7.96)	15 (5.28)
Relative Risk (RR) (95% CI)		0.6637 (0.3536, 1.2455)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2018
Odds Ratio (OR) (95% CI)		0.6449 (0.3293, 1.2631)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2009
Risk Difference (RD) (95% CI)		-0.0268 (-0.0674, 0.0139)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1966
Constipation	20 (6.92)	15 (5.28)
Relative Risk (RR) (95% CI)		0.7632 (0.3988, 1.4607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4145
Odds Ratio (OR) (95% CI)		0.7500 (0.3760, 1.4960)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4141

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0164 (-0.0555, 0.0228)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4120

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Abdominal pain upper	13 (4.50)	14 (4.93)
Relative Risk (RR) (95% CI)		1.0959 (0.5245, 2.2899)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8076
Odds Ratio (OR) (95% CI)		1.1009 (0.5080, 2.3855)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8076
Risk Difference (RD) (95% CI)		0.0043 (-0.0304, 0.0390)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8076
Vomiting	19 (6.57)	12 (4.23)
Relative Risk (RR) (95% CI)		0.6427 (0.3179, 1.2993)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2183
Odds Ratio (OR) (95% CI)		0.6269 (0.2985, 1.3167)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2175

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0235 (-0.0604, 0.0134)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2125

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Abdominal distension	5 (1.73)	6 (2.11)
Relative Risk (RR) (95% CI)		1.2211 (0.3769, 3.9560)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7391
Odds Ratio (OR) (95% CI)		1.2259 (0.3699, 4.0631)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7390
Risk Difference (RD) (95% CI)		0.0038 (-0.0187, 0.0263)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7388
Gastrooesophageal reflux disease	6 (2.08)	4 (1.41)
Relative Risk (RR) (95% CI)		0.6784 (0.1935, 2.3786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5444
Odds Ratio (OR) (95% CI)		0.6738 (0.1881, 2.4135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5442

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0067 (-0.0281, 0.0147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5409

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Flatulence	8 (2.77)	2 (0.70)
Relative Risk (RR) (95% CI)		0.2544 (0.0545, 1.1876)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0816
Odds Ratio (OR) (95% CI)		0.2491 (0.0524, 1.1834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0804
Risk Difference (RD) (95% CI)		-0.0206 (-0.0419, 0.0006)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0572
Investigations	94 (32.53)	104 (36.62)
Relative Risk (RR) (95% CI)		1.1259 (0.8983, 1.4111)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3035
Odds Ratio (OR) (95% CI)		1.1986 (0.8491, 1.6919)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3031
Risk Difference (RD) (95% CI)		0.0409 (-0.0369, 0.1188)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3025

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Alanine aminotransferase increased	18 (6.23)	25 (8.80)
Relative Risk (RR) (95% CI)		1.4133 (0.7887, 2.5327)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2451
Odds Ratio (OR) (95% CI)		1.4532 (0.7745, 2.7268)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2444
Risk Difference (RD) (95% CI)		0.0257 (-0.0174, 0.0689)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2423
Blood creatine phosphokinase increased	17 (5.88)	25 (8.80)
Relative Risk (RR) (95% CI)		1.4965 (0.8262, 2.7104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1835
Odds Ratio (OR) (95% CI)		1.5444 (0.8150, 2.9266)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1826

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0292 (-0.0135, 0.0719)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1799

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Aspartate aminotransferase increased	18 (6.23)	21 (7.39)
Relative Risk (RR) (95% CI)		1.1872 (0.6464, 2.1804)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5801
Odds Ratio (OR) (95% CI)		1.2022 (0.6263, 2.3074)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5800
Risk Difference (RD) (95% CI)		0.0117 (-0.0296, 0.0529)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5797
Bacterial test positive	13 (4.50)	7 (2.46)
Relative Risk (RR) (95% CI)		0.5479 (0.2219, 1.3533)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1922
Odds Ratio (OR) (95% CI)		0.5365 (0.2109, 1.3650)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1913

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0203 (-0.0503, 0.0096)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1831

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Blood alkaline phosphatase increased	6 (2.08)	7 (2.46)
Relative Risk (RR) (95% CI)		1.1872 (0.4040, 3.4892)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7551
Odds Ratio (OR) (95% CI)		1.1919 (0.3956, 3.5913)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7550
Risk Difference (RD) (95% CI)		0.0039 (-0.0205, 0.0283)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7549
Blood glucose increased	4 (1.38)	7 (2.46)
Relative Risk (RR) (95% CI)		1.7808 (0.5271, 6.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3529
Odds Ratio (OR) (95% CI)		1.8005 (0.5213, 6.2192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3524

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0108 (-0.0117, 0.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3467

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Gamma-glutamyltransferase increased	8 (2.77)	6 (2.11)
Relative Risk (RR) (95% CI)		0.7632 (0.2682, 2.1717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6125
Odds Ratio (OR) (95% CI)		0.7581 (0.2597, 2.2132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6124
Risk Difference (RD) (95% CI)		-0.0066 (-0.0318, 0.0187)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6109
SARS-CoV-2 test positive	8 (2.77)	6 (2.11)
Relative Risk (RR) (95% CI)		0.7632 (0.2682, 2.1717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6125
Odds Ratio (OR) (95% CI)		0.7581 (0.2597, 2.2132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6124

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0066 (-0.0318, 0.0187)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6109

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Weight decreased	5 (1.73)	6 (2.11)
Relative Risk (RR) (95% CI)		1.2211 (0.3769, 3.9560)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7391
Odds Ratio (OR) (95% CI)		1.2259 (0.3699, 4.0631)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7390
Risk Difference (RD) (95% CI)		0.0038 (-0.0187, 0.0263)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7388
Blood bilirubin increased	10 (3.46)	5 (1.76)
Relative Risk (RR) (95% CI)		0.5088 (0.1761, 1.4700)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2119
Odds Ratio (OR) (95% CI)		0.5000 (0.1687, 1.4816)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2111

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0170 (-0.0430, 0.0090)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2008

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
General disorders and administration site conditions	72 (24.91)	86 (30.28)
Relative Risk (RR) (95% CI)		1.2155 (0.9308, 1.5872)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1518
Odds Ratio (OR) (95% CI)		1.3091 (0.9064, 1.8906)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1510
Risk Difference (RD) (95% CI)		0.0537 (-0.0194, 0.1268)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1500
Fatigue	30 (10.38)	33 (11.62)
Relative Risk (RR) (95% CI)		1.1194 (0.7020, 1.7848)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6357
Odds Ratio (OR) (95% CI)		1.1351 (0.6721, 1.9169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6356
Risk Difference (RD) (95% CI)		0.0124 (-0.0389, 0.0636)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6355

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Pyrexia	29 (10.03)	28 (9.86)
Relative Risk (RR) (95% CI)		0.9825 (0.6002, 1.6083)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9441
Odds Ratio (OR) (95% CI)		0.9806 (0.5673, 1.6949)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9441
Risk Difference (RD) (95% CI)		-0.0018 (-0.0508, 0.0473)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9441
Pain	3 (1.04)	10 (3.52)
Relative Risk (RR) (95% CI)		3.3920 (0.9433, 12.1971)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0614
Odds Ratio (OR) (95% CI)		3.4793 (0.9475, 12.7769)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0603

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0248 (0.0004, 0.0492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0462

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Influenza like illness	5 (1.73)	7 (2.46)
Relative Risk (RR) (95% CI)		1.4246 (0.4575, 4.4363)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5414
Odds Ratio (OR) (95% CI)		1.4354 (0.4502, 4.5765)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5412
Risk Difference (RD) (95% CI)		0.0073 (-0.0161, 0.0308)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5396
Malaise	4 (1.38)	7 (2.46)
Relative Risk (RR) (95% CI)		1.7808 (0.5271, 6.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3529
Odds Ratio (OR) (95% CI)		1.8005 (0.5213, 6.2192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3524

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0108 (-0.0117, 0.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3467

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Nervous system disorders	64 (22.15)	72 (25.35)
Relative Risk (RR) (95% CI)		1.1448 (0.8530, 1.5364)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3676
Odds Ratio (OR) (95% CI)		1.1940 (0.8121, 1.7555)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3673
Risk Difference (RD) (95% CI)		0.0321 (-0.0376, 0.1017)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3669
Headache	41 (14.19)	51 (17.96)
Relative Risk (RR) (95% CI)		1.2658 (0.8682, 1.8456)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2205
Odds Ratio (OR) (95% CI)		1.3240 (0.8456, 2.0729)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2199
Risk Difference (RD) (95% CI)		0.0377 (-0.0224, 0.0978)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2187

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Dizziness	13 (4.50)	9 (3.17)
Relative Risk (RR) (95% CI)		0.7045 (0.3060, 1.6221)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4104
Odds Ratio (OR) (95% CI)		0.6948 (0.2922, 1.6521)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4100
Risk Difference (RD) (95% CI)		-0.0133 (-0.0447, 0.0181)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4067
Migraine	5 (1.73)	5 (1.76)
Relative Risk (RR) (95% CI)		1.0176 (0.2978, 3.4770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9778
Odds Ratio (OR) (95% CI)		1.0179 (0.2915, 3.5549)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9778

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0003 (-0.0211, 0.0218)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9778

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Skin and subcutaneous tissue disorders	52 (17.99)	68 (23.94)
Relative Risk (RR) (95% CI)		1.3307 (0.9646, 1.8358)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0818
Odds Ratio (OR) (95% CI)		1.4348 (0.9566, 2.1521)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0809
Risk Difference (RD) (95% CI)		0.0595 (-0.0070, 0.1260)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0795
Rash	13 (4.50)	25 (8.80)
Relative Risk (RR) (95% CI)		1.9569 (1.0217, 3.7481)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0429
Odds Ratio (OR) (95% CI)		2.0493 (1.0265, 4.0911)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0419
Risk Difference (RD) (95% CI)		0.0430 (0.0023, 0.0838)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0382

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Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Acne	12 (4.15)	11 (3.87)
Relative Risk (RR) (95% CI)		0.9328 (0.4185, 2.0793)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8649
Odds Ratio (OR) (95% CI)		0.9301 (0.4035, 2.1438)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8649
Risk Difference (RD) (95% CI)		-0.0028 (-0.0349, 0.0293)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8649
Pruritus	6 (2.08)	9 (3.17)
Relative Risk (RR) (95% CI)		1.5264 (0.5505, 4.2327)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4164
Odds Ratio (OR) (95% CI)		1.5436 (0.5422, 4.3946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4160

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0109 (-0.0152, 0.0371)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4132

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Alopecia	6 (2.08)	5 (1.76)
Relative Risk (RR) (95% CI)		0.8480 (0.2618, 2.7472)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7834
Odds Ratio (OR) (95% CI)		0.8453 (0.2550, 2.8016)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7834
Risk Difference (RD) (95% CI)		-0.0032 (-0.0256, 0.0193)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7830
Musculoskeletal and connective tissue disorders	71 (24.57)	55 (19.37)
Relative Risk (RR) (95% CI)		0.7883 (0.5772, 1.0766)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1346
Odds Ratio (OR) (95% CI)		0.7374 (0.4953, 1.0978)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1336
Risk Difference (RD) (95% CI)		-0.0520 (-0.1197, 0.0156)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1318

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Back pain	15 (5.19)	16 (5.63)
Relative Risk (RR) (95% CI)		1.0854 (0.5471, 2.1535)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8145
Odds Ratio (OR) (95% CI)		1.0905 (0.5286, 2.2500)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8145
Risk Difference (RD) (95% CI)		0.0044 (-0.0326, 0.0415)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8145
Arthralgia	25 (8.65)	14 (4.93)
Relative Risk (RR) (95% CI)		0.5699 (0.3025, 1.0736)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0818
Odds Ratio (OR) (95% CI)		0.5476 (0.2785, 1.0764)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0807

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0372 (-0.0782, 0.0038)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0756

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Myalgia	7 (2.42)	10 (3.52)
Relative Risk (RR) (95% CI)		1.4537 (0.5611, 3.7660)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4411
Odds Ratio (OR) (95% CI)		1.4703 (0.5518, 3.9178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4408
Risk Difference (RD) (95% CI)		0.0110 (-0.0168, 0.0388)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4387
Pain in extremity	7 (2.42)	6 (2.11)
Relative Risk (RR) (95% CI)		0.8722 (0.2968, 2.5635)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8037
Odds Ratio (OR) (95% CI)		0.8695 (0.2886, 2.6197)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8037

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0031 (-0.0275, 0.0213)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8034

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Musculoskeletal chest pain	7 (2.42)	4 (1.41)
Relative Risk (RR) (95% CI)		0.5815 (0.1721, 1.9647)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3828
Odds Ratio (OR) (95% CI)		0.5755 (0.1666, 1.9878)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3823
Risk Difference (RD) (95% CI)		-0.0101 (-0.0325, 0.0123)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3752
Injury, poisoning and procedural complications	53 (18.34)	46 (16.20)
Relative Risk (RR) (95% CI)		0.8832 (0.6166, 1.2652)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4982
Odds Ratio (OR) (95% CI)		0.8606 (0.5576, 1.3284)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4980
Risk Difference (RD) (95% CI)		-0.0214 (-0.0833, 0.0404)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4974

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Psychiatric disorders	36 (12.46)	41 (14.44)
Relative Risk (RR) (95% CI)		1.1589 (0.7640, 1.7579)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4877
Odds Ratio (OR) (95% CI)		1.1858 (0.7330, 1.9183)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4875
Risk Difference (RD) (95% CI)		0.0198 (-0.0361, 0.0757)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4873
Anxiety	6 (2.08)	16 (5.63)
Relative Risk (RR) (95% CI)		2.7136 (1.0773, 6.8356)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0342
Odds Ratio (OR) (95% CI)		2.8159 (1.0858, 7.3032)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0332
Risk Difference (RD) (95% CI)		0.0356 (0.0041, 0.0670)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0266

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Insomnia	14 (4.84)	11 (3.87)
Relative Risk (RR) (95% CI)		0.7995 (0.3693, 1.7312)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5703
Odds Ratio (OR) (95% CI)		0.7915 (0.3531, 1.7743)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5702
Risk Difference (RD) (95% CI)		-0.0097 (-0.0431, 0.0237)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5689
Depression	3 (1.04)	10 (3.52)
Relative Risk (RR) (95% CI)		3.3920 (0.9433, 12.1971)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0614
Odds Ratio (OR) (95% CI)		3.4793 (0.9475, 12.7769)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0603

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0248 (0.0004, 0.0492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0462

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Metabolism and nutrition disorders	25 (8.65)	25 (8.80)
Relative Risk (RR) (95% CI)		1.0176 (0.5992, 1.7282)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9485
Odds Ratio (OR) (95% CI)		1.0193 (0.5706, 1.8210)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9485
Risk Difference (RD) (95% CI)		0.0015 (-0.0447, 0.0477)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9485
Decreased appetite	8 (2.77)	3 (1.06)
Relative Risk (RR) (95% CI)		0.3816 (0.1023, 1.4239)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1516
Odds Ratio (OR) (95% CI)		0.3750 (0.0985, 1.4281)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1505
Risk Difference (RD) (95% CI)		-0.0171 (-0.0395, 0.0052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1332

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
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Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Eye disorders	18 (6.23)	17 (5.99)
Relative Risk (RR) (95% CI)		0.9611 (0.5056, 1.8269)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9036
Odds Ratio (OR) (95% CI)		0.9586 (0.4837, 1.8999)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9036
Risk Difference (RD) (95% CI)		-0.0024 (-0.0416, 0.0368)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9035
Renal and urinary disorders	15 (5.19)	10 (3.52)
Relative Risk (RR) (95% CI)		0.6784 (0.3100, 1.4847)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3316
Odds Ratio (OR) (95% CI)		0.6667 (0.2944, 1.5099)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3310
Risk Difference (RD) (95% CI)		-0.0167 (-0.0501, 0.0167)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3269

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Nephrolithiasis	6 (2.08)	4 (1.41)
Relative Risk (RR) (95% CI)		0.6784 (0.1935, 2.3786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5444
Odds Ratio (OR) (95% CI)		0.6738 (0.1881, 2.4135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5442
Risk Difference (RD) (95% CI)		-0.0067 (-0.0281, 0.0147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5409
Reproductive system and breast disorders	19 (6.57)	10 (3.52)
Relative Risk (RR) (95% CI)		0.5356 (0.2535, 1.1316)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1018
Odds Ratio (OR) (95% CI)		0.5186 (0.2368, 1.1359)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1007
Risk Difference (RD) (95% CI)		-0.0305 (-0.0663, 0.0052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0939

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Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Ear and labyrinth disorders	11 (3.81)	9 (3.17)
Relative Risk (RR) (95% CI)		0.8326 (0.3504, 1.9786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6782
Odds Ratio (OR) (95% CI)		0.8271 (0.3374, 2.0274)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6782
Risk Difference (RD) (95% CI)		-0.0064 (-0.0364, 0.0237)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6775
Congenital, familial and genetic disorders	5 (1.73)	8 (2.82)
Relative Risk (RR) (95% CI)		1.6282 (0.5391, 4.9172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3874
Odds Ratio (OR) (95% CI)		1.6464 (0.5321, 5.0944)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3870
Risk Difference (RD) (95% CI)		0.0109 (-0.0136, 0.0353)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3830

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Immune system disorders	8 (2.77)	8 (2.82)
Relative Risk (RR) (95% CI)		1.0176 (0.3872, 2.6742)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9718
Odds Ratio (OR) (95% CI)		1.0181 (0.3768, 2.7509)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9718
Risk Difference (RD) (95% CI)		0.0005 (-0.0265, 0.0275)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9718
Seasonal allergy	6 (2.08)	7 (2.46)
Relative Risk (RR) (95% CI)		1.1872 (0.4040, 3.4892)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7551
Odds Ratio (OR) (95% CI)		1.1919 (0.3956, 3.5913)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7550
Risk Difference (RD) (95% CI)		0.0039 (-0.0205, 0.0283)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7549

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Cardiac disorders	4 (1.38)	7 (2.46)
Relative Risk (RR) (95% CI)		1.7808 (0.5271, 6.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3529
Odds Ratio (OR) (95% CI)		1.8005 (0.5213, 6.2192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3524
Risk Difference (RD) (95% CI)		0.0108 (-0.0117, 0.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3467
Vascular disorders	9 (3.11)	5 (1.76)
Relative Risk (RR) (95% CI)		0.5653 (0.1918, 1.6662)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3010
Odds Ratio (OR) (95% CI)		0.5575 (0.1845, 1.6846)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3004
Risk Difference (RD) (95% CI)		-0.0135 (-0.0387, 0.0117)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2924

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Hepatobiliary disorders	9 (3.11)	4 (1.41)
Relative Risk (RR) (95% CI)		0.4523 (0.1409, 1.4519)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1824
Odds Ratio (OR) (95% CI)		0.4444 (0.1353, 1.4600)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1814
Risk Difference (RD) (95% CI)		-0.0171 (-0.0413, 0.0072)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1683

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with any TEAEs	271 (93.77)	274 (96.48)
Relative Risk (RR) (95% CI)		1.0289 (0.9914, 1.0678)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1327
Odds Ratio (OR) (95% CI)		1.8199 (0.8251, 4.0142)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1379
Risk Difference (RD) (95% CI)		0.0271 (-0.0081, 0.0622)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1312
Grade 1/Mild	89 (30.80)	103 (36.27)
Relative Risk (RR) (95% CI)		1.1777 (0.9342, 1.4846)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1664
Odds Ratio (OR) (95% CI)		1.2788 (0.9032, 1.8105)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1657

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0547 (-0.0225, 0.1319)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1648

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	153 (52.94)	147 (51.76)
Relative Risk (RR) (95% CI)		0.9777 (0.8363, 1.1431)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7773
Odds Ratio (OR) (95% CI)		0.9538 (0.6871, 1.3239)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7772
Risk Difference (RD) (95% CI)		-0.0118 (-0.0936, 0.0700)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7772
Grade 3/Severe	28 (9.69)	24 (8.45)
Relative Risk (RR) (95% CI)		0.8722 (0.5185, 1.4672)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6064
Odds Ratio (OR) (95% CI)		0.8604 (0.4858, 1.5240)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6063

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0124 (-0.0594, 0.0346)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6057

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Infections and infestations	208 (71.97)	199 (70.07)
Relative Risk (RR) (95% CI)		0.9736 (0.8768, 1.0810)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6160
Odds Ratio (OR) (95% CI)		0.9117 (0.6354, 1.3082)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6159
Risk Difference (RD) (95% CI)		-0.0190 (-0.0933, 0.0553)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6158
Grade 1/Mild	102 (35.29)	108 (38.03)
Relative Risk (RR) (95% CI)		1.0775 (0.8686, 1.3365)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4973
Odds Ratio (OR) (95% CI)		1.1250 (0.8007, 1.5806)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4972

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0273 (-0.0515, 0.1062)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4970

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	100 (34.60)	86 (30.28)
Relative Risk (RR) (95% CI)		0.8751 (0.6903, 1.1094)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2705
Odds Ratio (OR) (95% CI)		0.8209 (0.5782, 1.1654)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2697
Risk Difference (RD) (95% CI)		-0.0432 (-0.1198, 0.0334)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2688
Grade 3/Severe	5 (1.73)	5 (1.76)
Relative Risk (RR) (95% CI)		1.0176 (0.2978, 3.4770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9778
Odds Ratio (OR) (95% CI)		1.0179 (0.2915, 3.5549)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9778

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0003 (-0.0211, 0.0218)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9778

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
COVID-19	73 (25.26)	58 (20.42)
Relative Risk (RR) (95% CI)		0.8085 (0.5969, 1.0951)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1697
Odds Ratio (OR) (95% CI)		0.7594 (0.5131, 1.1238)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1687
Risk Difference (RD) (95% CI)		-0.0484 (-0.1170, 0.0202)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1671
Grade 1/Mild	47 (16.26)	37 (13.03)
Relative Risk (RR) (95% CI)		0.8011 (0.5378, 1.1932)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2753
Odds Ratio (OR) (95% CI)		0.7713 (0.4841, 1.2289)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2746

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0323 (-0.0902, 0.0255)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2728

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	25 (8.65)	21 (7.39)
Relative Risk (RR) (95% CI)		0.8548 (0.4899, 1.4913)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5806
Odds Ratio (OR) (95% CI)		0.8432 (0.4606, 1.5437)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5804
Risk Difference (RD) (95% CI)		-0.0126 (-0.0570, 0.0319)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5797
Grade 3/Severe	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Nasopharyngitis	60 (20.76)	57 (20.07)
Relative Risk (RR) (95% CI)		0.9667 (0.6996, 1.3359)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8375
Odds Ratio (OR) (95% CI)		0.9584 (0.6384, 1.4388)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8375
Risk Difference (RD) (95% CI)		-0.0069 (-0.0729, 0.0591)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8375
Grade 1/Mild	39 (13.49)	49 (17.25)
Relative Risk (RR) (95% CI)		1.2785 (0.8679, 1.8835)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2138
Odds Ratio (OR) (95% CI)		1.3366 (0.8465, 2.1104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2131

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0376 (-0.0214, 0.0966)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2119

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	21 (7.27)	8 (2.82)
Relative Risk (RR) (95% CI)		0.3877 (0.1746, 0.8608)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0199
Odds Ratio (OR) (95% CI)		0.3699 (0.1611, 0.8496)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0191
Risk Difference (RD) (95% CI)		-0.0445 (-0.0801, -0.0089)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0142
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Upper respiratory tract infection	40 (13.84)	55 (19.37)
Relative Risk (RR) (95% CI)		1.3992 (0.9637, 2.0316)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0775
Odds Ratio (OR) (95% CI)		1.4951 (0.9580, 2.3332)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0765
Risk Difference (RD) (95% CI)		0.0553 (-0.0056, 0.1161)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0749
Grade 1/Mild	27 (9.34)	40 (14.08)
Relative Risk (RR) (95% CI)		1.5076 (0.9518, 2.3878)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0802
Odds Ratio (OR) (95% CI)		1.5908 (0.9473, 2.6714)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0792

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0474 (-0.0051, 0.1000)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0770

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	13 (4.50)	15 (5.28)
Relative Risk (RR) (95% CI)		1.1742 (0.5690, 2.4229)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6640
Odds Ratio (OR) (95% CI)		1.1839 (0.5529, 2.5351)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6639
Risk Difference (RD) (95% CI)		0.0078 (-0.0275, 0.0432)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6638
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Influenza	16 (5.54)	33 (11.62)
Relative Risk (RR) (95% CI)		2.0988 (1.1820, 3.7268)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0114
Odds Ratio (OR) (95% CI)		2.2433 (1.2053, 4.1750)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0108
Risk Difference (RD) (95% CI)		0.0608 (0.0152, 0.1065)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0090
Grade 1/Mild	6 (2.08)	14 (4.93)
Relative Risk (RR) (95% CI)		2.3744 (0.9254, 6.0921)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0721
Odds Ratio (OR) (95% CI)		2.4457 (0.9264, 6.4567)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0710

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0285 (-0.0015, 0.0586)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0629

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	9 (3.11)	17 (5.99)
Relative Risk (RR) (95% CI)		1.9221 (0.8713, 4.2403)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1055
Odds Ratio (OR) (95% CI)		1.9809 (0.8679, 4.5208)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1045
Risk Difference (RD) (95% CI)		0.0287 (-0.0054, 0.0628)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0987
Grade 3/Severe	1 (0.35)	2 (0.70)
Relative Risk (RR) (95% CI)		2.0352 (0.1856, 22.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		2.0426 (0.1842, 22.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0036 (-0.0083, 0.0154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5535

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Viral upper respiratory tract infection	17 (5.88)	20 (7.04)
Relative Risk (RR) (95% CI)		1.1972 (0.6405, 2.2377)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5728
Odds Ratio (OR) (95% CI)		1.2121 (0.6213, 2.3649)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5727
Risk Difference (RD) (95% CI)		0.0116 (-0.0287, 0.0519)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5724
Grade 1/Mild	15 (5.19)	15 (5.28)
Relative Risk (RR) (95% CI)		1.0176 (0.5070, 2.0424)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9608
Odds Ratio (OR) (95% CI)		1.0186 (0.4883, 2.1246)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9608

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0009 (-0.0356, 0.0374)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9608

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	5 (1.76)
Relative Risk (RR) (95% CI)		2.5440 (0.4976, 13.0055)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2620
Odds Ratio (OR) (95% CI)		2.5717 (0.4948, 13.3651)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2613
Risk Difference (RD) (95% CI)		0.0107 (-0.0074, 0.0287)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2456
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Sinusitis	26 (9.00)	9 (3.17)
Relative Risk (RR) (95% CI)		0.3522 (0.1680, 0.7384)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0057
Odds Ratio (OR) (95% CI)		0.3310 (0.1523, 0.7197)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0053
Risk Difference (RD) (95% CI)		-0.0583 (-0.0970, -0.0195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0032
Grade 1/Mild	17 (5.88)	5 (1.76)
Relative Risk (RR) (95% CI)		0.2993 (0.1119, 0.8003)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0162
Odds Ratio (OR) (95% CI)		0.2867 (0.1043, 0.7881)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0154

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0412 (-0.0724, -0.0101)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0095

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	9 (3.11)	4 (1.41)
Relative Risk (RR) (95% CI)		0.4523 (0.1409, 1.4519)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1824
Odds Ratio (OR) (95% CI)		0.4444 (0.1353, 1.4600)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1814
Risk Difference (RD) (95% CI)		-0.0171 (-0.0413, 0.0072)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1683
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Urinary tract infection	10 (3.46)	9 (3.17)
Relative Risk (RR) (95% CI)		0.9158 (0.3778, 2.2202)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8457
Odds Ratio (OR) (95% CI)		0.9131 (0.3654, 2.2816)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8457
Risk Difference (RD) (95% CI)		-0.0029 (-0.0322, 0.0264)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8456
Grade 1/Mild	6 (2.08)	6 (2.11)
Relative Risk (RR) (95% CI)		1.0176 (0.3321, 3.1178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9756
Odds Ratio (OR) (95% CI)		1.0180 (0.3244, 3.1946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9756

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0004 (-0.0231, 0.0238)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9756

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	4 (1.38)	3 (1.06)
Relative Risk (RR) (95% CI)		0.7632 (0.1724, 3.3795)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7219
Odds Ratio (OR) (95% CI)		0.7607 (0.1687, 3.4296)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7218
Risk Difference (RD) (95% CI)		-0.0033 (-0.0212, 0.0147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7207
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Rhinitis	11 (3.81)	8 (2.82)
Relative Risk (RR) (95% CI)		0.7401 (0.3021, 1.8128)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5102
Odds Ratio (OR) (95% CI)		0.7325 (0.2902, 1.8489)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5100
Risk Difference (RD) (95% CI)		-0.0099 (-0.0392, 0.0194)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5077
Grade 1/Mild	9 (3.11)	8 (2.82)
Relative Risk (RR) (95% CI)		0.9045 (0.3540, 2.3114)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8340
Odds Ratio (OR) (95% CI)		0.9018 (0.3430, 2.3712)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8340

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0030 (-0.0307, 0.0248)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8338

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0069 (-0.0165, 0.0026)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1559
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Bronchitis	8 (2.77)	7 (2.46)
Relative Risk (RR) (95% CI)		0.8904 (0.3272, 2.4230)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8202
Odds Ratio (OR) (95% CI)		0.8876 (0.3176, 2.4810)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8202
Risk Difference (RD) (95% CI)		-0.0030 (-0.0292, 0.0231)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8200
Grade 1/Mild	3 (1.04)	2 (0.70)
Relative Risk (RR) (95% CI)		0.6784 (0.1142, 4.0296)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6695
Odds Ratio (OR) (95% CI)		0.6761 (0.1121, 4.0770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6694

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0033 (-0.0185, 0.0119)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6669

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	5 (1.73)	5 (1.76)
Relative Risk (RR) (95% CI)		1.0176 (0.2978, 3.4770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9778
Odds Ratio (OR) (95% CI)		1.0179 (0.2915, 3.5549)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9778
Risk Difference (RD) (95% CI)		0.0003 (-0.0211, 0.0218)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9778
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Gastroenteritis	4 (1.38)	7 (2.46)
Relative Risk (RR) (95% CI)		1.7808 (0.5271, 6.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3529
Odds Ratio (OR) (95% CI)		1.8005 (0.5213, 6.2192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3524
Risk Difference (RD) (95% CI)		0.0108 (-0.0117, 0.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3467
Grade 1/Mild	2 (0.69)	6 (2.11)
Relative Risk (RR) (95% CI)		3.0528 (0.6214, 14.9988)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1694
Odds Ratio (OR) (95% CI)		3.0971 (0.6198, 15.4754)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1684

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0142 (-0.0051, 0.0335)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1483

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	1 (0.35)
Relative Risk (RR) (95% CI)		0.5088 (0.0464, 5.5799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5803
Odds Ratio (OR) (95% CI)		0.5071 (0.0457, 5.6235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5801
Risk Difference (RD) (95% CI)		-0.0034 (-0.0152, 0.0084)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5717
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Conjunctivitis	12 (4.15)	5 (1.76)
Relative Risk (RR) (95% CI)		0.4240 (0.1513, 1.1881)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1026
Odds Ratio (OR) (95% CI)		0.4137 (0.1438, 1.1898)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1015
Risk Difference (RD) (95% CI)		-0.0239 (-0.0515, 0.0037)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0897
Grade 1/Mild	5 (1.73)	4 (1.41)
Relative Risk (RR) (95% CI)		0.8141 (0.2209, 3.0007)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7573
Odds Ratio (OR) (95% CI)		0.8114 (0.2157, 3.0531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7573

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0032 (-0.0236, 0.0171)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7566

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	7 (2.42)	1 (0.35)
Relative Risk (RR) (95% CI)		0.1454 (0.0180, 1.1740)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0704
Odds Ratio (OR) (95% CI)		0.1424 (0.0174, 1.1645)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0691
Risk Difference (RD) (95% CI)		-0.0207 (-0.0397, -0.0017)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0329
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Pharyngitis	8 (2.77)	5 (1.76)
Relative Risk (RR) (95% CI)		0.6360 (0.2106, 1.9208)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4223
Odds Ratio (OR) (95% CI)		0.6295 (0.2034, 1.9478)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4219
Risk Difference (RD) (95% CI)		-0.0101 (-0.0344, 0.0142)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4169
Grade 1/Mild	5 (1.73)	4 (1.41)
Relative Risk (RR) (95% CI)		0.8141 (0.2209, 3.0007)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7573
Odds Ratio (OR) (95% CI)		0.8114 (0.2157, 3.0531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7573

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0032 (-0.0236, 0.0171)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7566

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	1 (0.35)
Relative Risk (RR) (95% CI)		0.3392 (0.0355, 3.2416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3478
Odds Ratio (OR) (95% CI)		0.3369 (0.0348, 3.2578)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3473
Risk Difference (RD) (95% CI)		-0.0069 (-0.0204, 0.0067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3216
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Vulvovaginal mycotic infection	7 (2.42)	5 (1.76)
Relative Risk (RR) (95% CI)		0.7269 (0.2334, 2.2634)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5820
Odds Ratio (OR) (95% CI)		0.7220 (0.2264, 2.3019)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5819
Risk Difference (RD) (95% CI)		-0.0066 (-0.0300, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5797
Grade 1/Mild	2 (0.69)	2 (0.70)
Relative Risk (RR) (95% CI)		1.0176 (0.1443, 7.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9860
Odds Ratio (OR) (95% CI)		1.0177 (0.1424, 7.2748)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9860

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0001 (-0.0135, 0.0138)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9860

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	5 (1.73)	3 (1.06)
Relative Risk (RR) (95% CI)		0.6106 (0.1473, 2.5309)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4965
Odds Ratio (OR) (95% CI)		0.6064 (0.1436, 2.5616)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4962
Risk Difference (RD) (95% CI)		-0.0067 (-0.0259, 0.0124)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4908
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Otitis media	6 (2.08)	4 (1.41)
Relative Risk (RR) (95% CI)		0.6784 (0.1935, 2.3786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5444
Odds Ratio (OR) (95% CI)		0.6738 (0.1881, 2.4135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5442
Risk Difference (RD) (95% CI)		-0.0067 (-0.0281, 0.0147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5409
Grade 1/Mild	3 (1.04)	2 (0.70)
Relative Risk (RR) (95% CI)		0.6784 (0.1142, 4.0296)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6695
Odds Ratio (OR) (95% CI)		0.6761 (0.1121, 4.0770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6694

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0033 (-0.0185, 0.0119)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6669

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	2 (0.70)
Relative Risk (RR) (95% CI)		0.6784 (0.1142, 4.0296)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6695
Odds Ratio (OR) (95% CI)		0.6761 (0.1121, 4.0770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6694
Risk Difference (RD) (95% CI)		-0.0033 (-0.0185, 0.0119)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6669
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Pneumonia	8 (2.77)	4 (1.41)
Relative Risk (RR) (95% CI)		0.5088 (0.1549, 1.6708)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2654
Odds Ratio (OR) (95% CI)		0.5018 (0.1494, 1.6854)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2646
Risk Difference (RD) (95% CI)		-0.0136 (-0.0370, 0.0098)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2539
Grade 1/Mild	1 (0.35)	2 (0.70)
Relative Risk (RR) (95% CI)		2.0352 (0.1856, 22.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		2.0426 (0.1842, 22.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0036 (-0.0083, 0.0154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5535

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	4 (1.38)	2 (0.70)
Relative Risk (RR) (95% CI)		0.5088 (0.0939, 2.7560)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4331
Odds Ratio (OR) (95% CI)		0.5053 (0.0918, 2.7809)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4328
Risk Difference (RD) (95% CI)		-0.0068 (-0.0234, 0.0098)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4225
Grade 3/Severe	2 (0.69)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0069 (-0.0165, 0.0026)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1559

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Respiratory, thoracic and mediastinal disorders	153 (52.94)	145 (51.06)
Relative Risk (RR) (95% CI)		0.9644 (0.8239, 1.1288)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6517
Odds Ratio (OR) (95% CI)		0.9273 (0.6681, 1.2870)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6516
Risk Difference (RD) (95% CI)		-0.0188 (-0.1007, 0.0630)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6516
Grade 1/Mild	102 (35.29)	104 (36.62)
Relative Risk (RR) (95% CI)		1.0376 (0.8338, 1.2911)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7409
Odds Ratio (OR) (95% CI)		1.0593 (0.7530, 1.4901)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7409

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0133 (-0.0653, 0.0918)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7409

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	48 (16.61)	40 (14.08)
Relative Risk (RR) (95% CI)		0.8480 (0.5763, 1.2479)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4029
Odds Ratio (OR) (95% CI)		0.8231 (0.5218, 1.2984)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4025
Risk Difference (RD) (95% CI)		-0.0252 (-0.0842, 0.0337)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4015
Grade 3/Severe	3 (1.04)	1 (0.35)
Relative Risk (RR) (95% CI)		0.3392 (0.0355, 3.2416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3478
Odds Ratio (OR) (95% CI)		0.3369 (0.0348, 3.2578)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3473

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0069 (-0.0204, 0.0067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3216

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Cough	60 (20.76)	63 (22.18)
Relative Risk (RR) (95% CI)		1.0685 (0.7811, 1.4617)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6786
Odds Ratio (OR) (95% CI)		1.0880 (0.7301, 1.6214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6786
Risk Difference (RD) (95% CI)		0.0142 (-0.0530, 0.0815)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6786
Grade 1/Mild	44 (15.22)	50 (17.61)
Relative Risk (RR) (95% CI)		1.1564 (0.7983, 1.6751)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4422
Odds Ratio (OR) (95% CI)		1.1898 (0.7640, 1.8529)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4420

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0238 (-0.0368, 0.0845)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4416

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	15 (5.19)	13 (4.58)
Relative Risk (RR) (95% CI)		0.8819 (0.4274, 1.8199)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7339
Odds Ratio (OR) (95% CI)		0.8763 (0.4092, 1.8764)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7339
Risk Difference (RD) (95% CI)		-0.0061 (-0.0414, 0.0292)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7335
Grade 3/Severe	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Oropharyngeal pain	37 (12.80)	45 (15.85)
Relative Risk (RR) (95% CI)		1.2376 (0.8272, 1.8518)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2997
Odds Ratio (OR) (95% CI)		1.2824 (0.8018, 2.0509)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2992
Risk Difference (RD) (95% CI)		0.0304 (-0.0269, 0.0878)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2984
Grade 1/Mild	27 (9.34)	34 (11.97)
Relative Risk (RR) (95% CI)		1.2814 (0.7945, 2.0667)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3092
Odds Ratio (OR) (95% CI)		1.3197 (0.7736, 2.2514)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3087

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0263 (-0.0242, 0.0768)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3076

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	10 (3.46)	11 (3.87)
Relative Risk (RR) (95% CI)		1.1194 (0.4830, 2.5943)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7926
Odds Ratio (OR) (95% CI)		1.1242 (0.4698, 2.6900)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7926
Risk Difference (RD) (95% CI)		0.0041 (-0.0267, 0.0349)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7926
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Nasal congestion	23 (7.96)	29 (10.21)
Relative Risk (RR) (95% CI)		1.2831 (0.7612, 2.1629)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3495
Odds Ratio (OR) (95% CI)		1.3153 (0.7412, 2.3341)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3491
Risk Difference (RD) (95% CI)		0.0225 (-0.0245, 0.0696)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3480
Grade 1/Mild	21 (7.27)	27 (9.51)
Relative Risk (RR) (95% CI)		1.3084 (0.7577, 2.2592)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3349
Odds Ratio (OR) (95% CI)		1.3407 (0.7392, 2.4317)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3344

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0224 (-0.0230, 0.0678)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3332

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	2 (0.70)
Relative Risk (RR) (95% CI)		1.0176 (0.1443, 7.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9860
Odds Ratio (OR) (95% CI)		1.0177 (0.1424, 7.2748)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9860
Risk Difference (RD) (95% CI)		0.0001 (-0.0135, 0.0138)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9860
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Sputum increased	29 (10.03)	27 (9.51)
Relative Risk (RR) (95% CI)		0.9474 (0.5758, 1.5588)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8316
Odds Ratio (OR) (95% CI)		0.9419 (0.5425, 1.6355)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8316
Risk Difference (RD) (95% CI)		-0.0053 (-0.0539, 0.0433)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8316
Grade 1/Mild	21 (7.27)	17 (5.99)
Relative Risk (RR) (95% CI)		0.8238 (0.4440, 1.5285)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5388
Odds Ratio (OR) (95% CI)		0.8126 (0.4193, 1.5745)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5386

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0128 (-0.0535, 0.0279)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5375

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	8 (2.77)	10 (3.52)
Relative Risk (RR) (95% CI)		1.2720 (0.5094, 3.1764)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6064
Odds Ratio (OR) (95% CI)		1.2819 (0.4985, 3.2964)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6063
Risk Difference (RD) (95% CI)		0.0075 (-0.0211, 0.0361)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6057
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Sinus congestion	10 (3.46)	18 (6.34)
Relative Risk (RR) (95% CI)		1.8317 (0.8605, 3.8990)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1164
Odds Ratio (OR) (95% CI)		1.8880 (0.8559, 4.1643)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1154
Risk Difference (RD) (95% CI)		0.0288 (-0.0065, 0.0641)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1102
Grade 1/Mild	9 (3.11)	17 (5.99)
Relative Risk (RR) (95% CI)		1.9221 (0.8713, 4.2403)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1055
Odds Ratio (OR) (95% CI)		1.9809 (0.8679, 4.5208)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1045

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0287 (-0.0054, 0.0628)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0987

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Haemoptysis	22 (7.61)	17 (5.99)
Relative Risk (RR) (95% CI)		0.7863 (0.4267, 1.4492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4409
Odds Ratio (OR) (95% CI)		0.7727 (0.4013, 1.4880)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4406
Risk Difference (RD) (95% CI)		-0.0163 (-0.0574, 0.0249)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4389
Grade 1/Mild	11 (3.81)	12 (4.23)
Relative Risk (RR) (95% CI)		1.1101 (0.4980, 2.4745)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7984
Odds Ratio (OR) (95% CI)		1.1150 (0.4837, 2.5699)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7984

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0042 (-0.0280, 0.0363)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7984

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- [1] Relative risk from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	10 (3.46)	4 (1.41)
Relative Risk (RR) (95% CI)		0.4070 (0.1292, 1.2828)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1249
Odds Ratio (OR) (95% CI)		0.3986 (0.1235, 1.2859)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1238
Risk Difference (RD) (95% CI)		-0.0205 (-0.0457, 0.0046)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1096
Grade 3/Severe	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Productive cough	19 (6.57)	16 (5.63)
Relative Risk (RR) (95% CI)		0.8569 (0.4498, 1.6326)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6387
Odds Ratio (OR) (95% CI)		0.8484 (0.4272, 1.6850)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6386
Risk Difference (RD) (95% CI)		-0.0094 (-0.0486, 0.0298)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6380
Grade 1/Mild	16 (5.54)	13 (4.58)
Relative Risk (RR) (95% CI)		0.8268 (0.4052, 1.6872)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6013
Odds Ratio (OR) (95% CI)		0.8185 (0.3863, 1.7343)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6011

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0096 (-0.0454, 0.0263)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6002

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	3 (1.06)
Relative Risk (RR) (95% CI)		1.5264 (0.2570, 9.0666)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6418
Odds Ratio (OR) (95% CI)		1.5320 (0.2541, 9.2381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6417
Risk Difference (RD) (95% CI)		0.0036 (-0.0116, 0.0189)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6398
Grade 3/Severe	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Rhinorrhoea	22 (7.61)	16 (5.63)
Relative Risk (RR) (95% CI)		0.7401 (0.3970, 1.3796)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3435
Odds Ratio (OR) (95% CI)		0.7246 (0.3723, 1.4102)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3430
Risk Difference (RD) (95% CI)		-0.0198 (-0.0605, 0.0209)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3403
Grade 1/Mild	20 (6.92)	14 (4.93)
Relative Risk (RR) (95% CI)		0.7123 (0.3670, 1.3824)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3160
Odds Ratio (OR) (95% CI)		0.6974 (0.3451, 1.4094)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3154

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0199 (-0.0585, 0.0187)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3121

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	2 (0.70)
Relative Risk (RR) (95% CI)		1.0176 (0.1443, 7.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9860
Odds Ratio (OR) (95% CI)		1.0177 (0.1424, 7.2748)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9860
Risk Difference (RD) (95% CI)		0.0001 (-0.0135, 0.0138)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9860
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Dyspnoea	21 (7.27)	11 (3.87)
Relative Risk (RR) (95% CI)		0.5330 (0.2618, 1.0851)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0828
Odds Ratio (OR) (95% CI)		0.5142 (0.2432, 1.0872)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0817
Risk Difference (RD) (95% CI)		-0.0339 (-0.0713, 0.0035)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0754
Grade 1/Mild	11 (3.81)	9 (3.17)
Relative Risk (RR) (95% CI)		0.8326 (0.3504, 1.9786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6782
Odds Ratio (OR) (95% CI)		0.8271 (0.3374, 2.0274)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6782

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0064 (-0.0364, 0.0237)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6775

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	10 (3.46)	2 (0.70)
Relative Risk (RR) (95% CI)		0.2035 (0.0450, 0.9207)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0387
Odds Ratio (OR) (95% CI)		0.1979 (0.0430, 0.9112)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0376
Risk Difference (RD) (95% CI)		-0.0276 (-0.0508, -0.0044)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0199
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Lower respiratory tract congestion	5 (1.73)	9 (3.17)
Relative Risk (RR) (95% CI)		1.8317 (0.6215, 5.3985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2724
Odds Ratio (OR) (95% CI)		1.8589 (0.6152, 5.6165)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2718
Risk Difference (RD) (95% CI)		0.0144 (-0.0109, 0.0397)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2653
Grade 1/Mild	3 (1.04)	8 (2.82)
Relative Risk (RR) (95% CI)		2.7136 (0.7273, 10.1253)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1373
Odds Ratio (OR) (95% CI)		2.7633 (0.7256, 10.5233)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1363

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0178 (-0.0047, 0.0403)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1215

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	1 (0.35)
Relative Risk (RR) (95% CI)		0.5088 (0.0464, 5.5799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5803
Odds Ratio (OR) (95% CI)		0.5071 (0.0457, 5.6235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5801
Risk Difference (RD) (95% CI)		-0.0034 (-0.0152, 0.0084)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5717
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Respiration abnormal	7 (2.42)	9 (3.17)
Relative Risk (RR) (95% CI)		1.3084 (0.4940, 3.4654)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5886
Odds Ratio (OR) (95% CI)		1.3184 (0.4843, 3.5896)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5885
Risk Difference (RD) (95% CI)		0.0075 (-0.0195, 0.0345)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5878
Grade 1/Mild	3 (1.04)	8 (2.82)
Relative Risk (RR) (95% CI)		2.7136 (0.7273, 10.1253)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1373
Odds Ratio (OR) (95% CI)		2.7633 (0.7256, 10.5233)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1363

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0178 (-0.0047, 0.0403)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1215

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	4 (1.38)	1 (0.35)
Relative Risk (RR) (95% CI)		0.2544 (0.0286, 2.2622)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2195
Odds Ratio (OR) (95% CI)		0.2518 (0.0280, 2.2665)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2186
Risk Difference (RD) (95% CI)		-0.0103 (-0.0254, 0.0048)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1813
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Wheezing	7 (2.42)	8 (2.82)
Relative Risk (RR) (95% CI)		1.1630 (0.4274, 3.1647)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7675
Odds Ratio (OR) (95% CI)		1.1677 (0.4178, 3.2638)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7675
Risk Difference (RD) (95% CI)		0.0039 (-0.0222, 0.0301)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7674
Grade 1/Mild	6 (2.08)	5 (1.76)
Relative Risk (RR) (95% CI)		0.8480 (0.2618, 2.7472)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7834
Odds Ratio (OR) (95% CI)		0.8453 (0.2550, 2.8016)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7834

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0032 (-0.0256, 0.0193)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7830

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	3 (1.06)
Relative Risk (RR) (95% CI)		3.0528 (0.3194, 29.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3325
Odds Ratio (OR) (95% CI)		3.0747 (0.3179, 29.7357)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3320
Risk Difference (RD) (95% CI)		0.0071 (-0.0066, 0.0208)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3089
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Upper-airway cough syndrome	8 (2.77)	2 (0.70)
Relative Risk (RR) (95% CI)		0.2544 (0.0545, 1.1876)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0816
Odds Ratio (OR) (95% CI)		0.2491 (0.0524, 1.1834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0804
Risk Difference (RD) (95% CI)		-0.0206 (-0.0419, 0.0006)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0572
Grade 1/Mild	8 (2.77)	2 (0.70)
Relative Risk (RR) (95% CI)		0.2544 (0.0545, 1.1876)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0816
Odds Ratio (OR) (95% CI)		0.2491 (0.0524, 1.1834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0804

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0206 (-0.0419, 0.0006)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0572

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Gastrointestinal disorders	111 (38.41)	114 (40.14)
Relative Risk (RR) (95% CI)		1.0451 (0.8525, 1.2812)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6712
Odds Ratio (OR) (95% CI)		1.0754 (0.7689, 1.5039)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6711
Risk Difference (RD) (95% CI)		0.0173 (-0.0626, 0.0973)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6711
Grade 1/Mild	57 (19.72)	70 (24.65)
Relative Risk (RR) (95% CI)		1.2497 (0.9175, 1.7021)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1574
Odds Ratio (OR) (95% CI)		1.3314 (0.8961, 1.9781)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1566

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0492 (-0.0187, 0.1172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1554

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	49 (16.96)	40 (14.08)
Relative Risk (RR) (95% CI)		0.8307 (0.5657, 1.2198)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3440
Odds Ratio (OR) (95% CI)		0.8029 (0.5099, 1.2644)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3435
Risk Difference (RD) (95% CI)		-0.0287 (-0.0879, 0.0305)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3422
Grade 3/Severe	5 (1.73)	4 (1.41)
Relative Risk (RR) (95% CI)		0.8141 (0.2209, 3.0007)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7573
Odds Ratio (OR) (95% CI)		0.8114 (0.2157, 3.0531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7573

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0032 (-0.0236, 0.0171)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7566

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Diarrhoea	44 (15.22)	37 (13.03)
Relative Risk (RR) (95% CI)		0.8557 (0.5705, 1.2834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4512
Odds Ratio (OR) (95% CI)		0.8341 (0.5205, 1.3366)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4509
Risk Difference (RD) (95% CI)		-0.0220 (-0.0790, 0.0350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4500
Grade 1/Mild	31 (10.73)	30 (10.56)
Relative Risk (RR) (95% CI)		0.9848 (0.6127, 1.5827)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9495
Odds Ratio (OR) (95% CI)		0.9830 (0.5780, 1.6717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9495

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0016 (-0.0521, 0.0489)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9495

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	12 (4.15)	7 (2.46)
Relative Risk (RR) (95% CI)		0.5936 (0.2371, 1.4860)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2653
Odds Ratio (OR) (95% CI)		0.5833 (0.2263, 1.5037)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2646
Risk Difference (RD) (95% CI)		-0.0169 (-0.0461, 0.0124)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2578
Grade 3/Severe	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Nausea	13 (4.50)	22 (7.75)
Relative Risk (RR) (95% CI)		1.7221 (0.8849, 3.3513)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1096
Odds Ratio (OR) (95% CI)		1.7827 (0.8798, 3.6122)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1086
Risk Difference (RD) (95% CI)		0.0325 (-0.0067, 0.0717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1045
Grade 1/Mild	12 (4.15)	16 (5.63)
Relative Risk (RR) (95% CI)		1.3568 (0.6536, 2.8164)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4129
Odds Ratio (OR) (95% CI)		1.3781 (0.6399, 2.9677)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4125

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0148 (-0.0205, 0.0501)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4111

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	6 (2.11)
Relative Risk (RR) (95% CI)		6.1056 (0.7397, 50.3940)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0929
Odds Ratio (OR) (95% CI)		6.2158 (0.7436, 51.9617)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0917
Risk Difference (RD) (95% CI)		0.0177 (-0.0004, 0.0357)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0550
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Abdominal pain	23 (7.96)	15 (5.28)
Relative Risk (RR) (95% CI)		0.6637 (0.3536, 1.2455)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2018
Odds Ratio (OR) (95% CI)		0.6449 (0.3293, 1.2631)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2009
Risk Difference (RD) (95% CI)		-0.0268 (-0.0674, 0.0139)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1966
Grade 1/Mild	11 (3.81)	11 (3.87)
Relative Risk (RR) (95% CI)		1.0176 (0.4484, 2.3094)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9667
Odds Ratio (OR) (95% CI)		1.0183 (0.4343, 2.3879)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9667

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0007 (-0.0308, 0.0321)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9667

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	11 (3.81)	4 (1.41)
Relative Risk (RR) (95% CI)		0.3700 (0.1192, 1.1485)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0854
Odds Ratio (OR) (95% CI)		0.3610 (0.1136, 1.1475)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0842
Risk Difference (RD) (95% CI)		-0.0240 (-0.0499, 0.0020)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0704
Grade 3/Severe	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Constipation	20 (6.92)	15 (5.28)
Relative Risk (RR) (95% CI)		0.7632 (0.3988, 1.4607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4145
Odds Ratio (OR) (95% CI)		0.7500 (0.3760, 1.4960)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4141
Risk Difference (RD) (95% CI)		-0.0164 (-0.0555, 0.0228)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4120
Grade 1/Mild	10 (3.46)	7 (2.46)
Relative Risk (RR) (95% CI)		0.7123 (0.2750, 1.8454)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4849
Odds Ratio (OR) (95% CI)		0.7051 (0.2646, 1.8787)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4846

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0100 (-0.0377, 0.0178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4818

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	9 (3.11)	8 (2.82)
Relative Risk (RR) (95% CI)		0.9045 (0.3540, 2.3114)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8340
Odds Ratio (OR) (95% CI)		0.9018 (0.3430, 2.3712)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8340
Risk Difference (RD) (95% CI)		-0.0030 (-0.0307, 0.0248)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8338
Grade 3/Severe	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Abdominal pain upper	13 (4.50)	14 (4.93)
Relative Risk (RR) (95% CI)		1.0959 (0.5245, 2.2899)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8076
Odds Ratio (OR) (95% CI)		1.1009 (0.5080, 2.3855)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8076
Risk Difference (RD) (95% CI)		0.0043 (-0.0304, 0.0390)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8076
Grade 1/Mild	8 (2.77)	10 (3.52)
Relative Risk (RR) (95% CI)		1.2720 (0.5094, 3.1764)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6064
Odds Ratio (OR) (95% CI)		1.2819 (0.4985, 3.2964)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6063

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0075 (-0.0211, 0.0361)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6057

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	5 (1.73)	3 (1.06)
Relative Risk (RR) (95% CI)		0.6106 (0.1473, 2.5309)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4965
Odds Ratio (OR) (95% CI)		0.6064 (0.1436, 2.5616)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4962
Risk Difference (RD) (95% CI)		-0.0067 (-0.0259, 0.0124)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4908
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Vomiting	19 (6.57)	12 (4.23)
Relative Risk (RR) (95% CI)		0.6427 (0.3179, 1.2993)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2183
Odds Ratio (OR) (95% CI)		0.6269 (0.2985, 1.3167)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2175
Risk Difference (RD) (95% CI)		-0.0235 (-0.0604, 0.0134)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2125
Grade 1/Mild	10 (3.46)	10 (3.52)
Relative Risk (RR) (95% CI)		1.0176 (0.4301, 2.4074)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9683
Odds Ratio (OR) (95% CI)		1.0182 (0.4172, 2.4851)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9683

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0006 (-0.0294, 0.0307)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9683

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	9 (3.11)	2 (0.70)
Relative Risk (RR) (95% CI)		0.2261 (0.0493, 1.0375)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0558
Odds Ratio (OR) (95% CI)		0.2206 (0.0473, 1.0303)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0546
Risk Difference (RD) (95% CI)		-0.0241 (-0.0464, -0.0018)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0339
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Abdominal distension	5 (1.73)	6 (2.11)
Relative Risk (RR) (95% CI)		1.2211 (0.3769, 3.9560)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7391
Odds Ratio (OR) (95% CI)		1.2259 (0.3699, 4.0631)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7390
Risk Difference (RD) (95% CI)		0.0038 (-0.0187, 0.0263)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7388
Grade 1/Mild	2 (0.69)	5 (1.76)
Relative Risk (RR) (95% CI)		2.5440 (0.4976, 13.0055)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2620
Odds Ratio (OR) (95% CI)		2.5717 (0.4948, 13.3651)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2613

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0107 (-0.0074, 0.0287)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2456

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	1 (0.35)
Relative Risk (RR) (95% CI)		0.3392 (0.0355, 3.2416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3478
Odds Ratio (OR) (95% CI)		0.3369 (0.0348, 3.2578)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3473
Risk Difference (RD) (95% CI)		-0.0069 (-0.0204, 0.0067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3216
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Gastrooesophageal reflux disease	6 (2.08)	4 (1.41)
Relative Risk (RR) (95% CI)		0.6784 (0.1935, 2.3786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5444
Odds Ratio (OR) (95% CI)		0.6738 (0.1881, 2.4135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5442
Risk Difference (RD) (95% CI)		-0.0067 (-0.0281, 0.0147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5409
Grade 1/Mild	3 (1.04)	3 (1.06)
Relative Risk (RR) (95% CI)		1.0176 (0.2071, 4.9996)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9829
Odds Ratio (OR) (95% CI)		1.0178 (0.2037, 5.0855)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9829

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0002 (-0.0165, 0.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9829

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	1 (0.35)
Relative Risk (RR) (95% CI)		0.5088 (0.0464, 5.5799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5803
Odds Ratio (OR) (95% CI)		0.5071 (0.0457, 5.6235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5801
Risk Difference (RD) (95% CI)		-0.0034 (-0.0152, 0.0084)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5717
Grade 3/Severe	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Flatulence	8 (2.77)	2 (0.70)
Relative Risk (RR) (95% CI)		0.2544 (0.0545, 1.1876)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0816
Odds Ratio (OR) (95% CI)		0.2491 (0.0524, 1.1834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0804
Risk Difference (RD) (95% CI)		-0.0206 (-0.0419, 0.0006)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0572
Grade 1/Mild	5 (1.73)	2 (0.70)
Relative Risk (RR) (95% CI)		0.4070 (0.0796, 2.0809)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2803
Odds Ratio (OR) (95% CI)		0.4028 (0.0775, 2.0935)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2796

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0103 (-0.0282, 0.0076)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2614

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0104 (-0.0221, 0.0013)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0817
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Investigations	94 (32.53)	104 (36.62)
Relative Risk (RR) (95% CI)		1.1259 (0.8983, 1.4111)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3035
Odds Ratio (OR) (95% CI)		1.1986 (0.8491, 1.6919)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3031
Risk Difference (RD) (95% CI)		0.0409 (-0.0369, 0.1188)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3025
Grade 1/Mild	55 (19.03)	64 (22.54)
Relative Risk (RR) (95% CI)		1.1841 (0.8590, 1.6323)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3021
Odds Ratio (OR) (95% CI)		1.2377 (0.8258, 1.8550)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3017

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0350 (-0.0314, 0.1014)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3010

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	34 (11.76)	35 (12.32)
Relative Risk (RR) (95% CI)		1.0475 (0.6729, 1.6308)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8371
Odds Ratio (OR) (95% CI)		1.0542 (0.6374, 1.7437)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8371
Risk Difference (RD) (95% CI)		0.0056 (-0.0477, 0.0589)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8371
Grade 3/Severe	5 (1.73)	5 (1.76)
Relative Risk (RR) (95% CI)		1.0176 (0.2978, 3.4770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9778
Odds Ratio (OR) (95% CI)		1.0179 (0.2915, 3.5549)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9778

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0003 (-0.0211, 0.0218)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9778

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Alanine aminotransferase increased	18 (6.23)	25 (8.80)
Relative Risk (RR) (95% CI)		1.4133 (0.7887, 2.5327)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2451
Odds Ratio (OR) (95% CI)		1.4532 (0.7745, 2.7268)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2444
Risk Difference (RD) (95% CI)		0.0257 (-0.0174, 0.0689)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2423
Grade 1/Mild	8 (2.77)	15 (5.28)
Relative Risk (RR) (95% CI)		1.9080 (0.8218, 4.4298)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1328
Odds Ratio (OR) (95% CI)		1.9586 (0.8171, 4.6948)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1318

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0251 (-0.0070, 0.0573)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1256

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	10 (3.46)	6 (2.11)
Relative Risk (RR) (95% CI)		0.6106 (0.2249, 1.6577)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3330
Odds Ratio (OR) (95% CI)		0.6022 (0.2159, 1.6794)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3324
Risk Difference (RD) (95% CI)		-0.0135 (-0.0404, 0.0134)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3262
Grade 3/Severe	0	4 (1.41)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0141 (0.0004, 0.0278)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0440

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Blood creatine phosphokinase increased	17 (5.88)	25 (8.80)
Relative Risk (RR) (95% CI)		1.4965 (0.8262, 2.7104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1835
Odds Ratio (OR) (95% CI)		1.5444 (0.8150, 2.9266)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1826
Risk Difference (RD) (95% CI)		0.0292 (-0.0135, 0.0719)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1799
Grade 1/Mild	10 (3.46)	16 (5.63)
Relative Risk (RR) (95% CI)		1.6282 (0.7517, 3.5268)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2164
Odds Ratio (OR) (95% CI)		1.6657 (0.7427, 3.7356)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2157

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0217 (-0.0124, 0.0558)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2116

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	6 (2.08)	8 (2.82)
Relative Risk (RR) (95% CI)		1.3568 (0.4768, 3.8609)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5674
Odds Ratio (OR) (95% CI)		1.3671 (0.4683, 3.9914)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5673
Risk Difference (RD) (95% CI)		0.0074 (-0.0179, 0.0327)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5662
Grade 3/Severe	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Aspartate aminotransferase increased	18 (6.23)	21 (7.39)
Relative Risk (RR) (95% CI)		1.1872 (0.6464, 2.1804)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5801
Odds Ratio (OR) (95% CI)		1.2022 (0.6263, 2.3074)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5800
Risk Difference (RD) (95% CI)		0.0117 (-0.0296, 0.0529)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5797
Grade 1/Mild	10 (3.46)	11 (3.87)
Relative Risk (RR) (95% CI)		1.1194 (0.4830, 2.5943)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7926
Odds Ratio (OR) (95% CI)		1.1242 (0.4698, 2.6900)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7926

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0041 (-0.0267, 0.0349)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7926

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	8 (2.77)	8 (2.82)
Relative Risk (RR) (95% CI)		1.0176 (0.3872, 2.6742)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9718
Odds Ratio (OR) (95% CI)		1.0181 (0.3768, 2.7509)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9718
Risk Difference (RD) (95% CI)		0.0005 (-0.0265, 0.0275)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9718
Grade 3/Severe	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Bacterial test positive	13 (4.50)	7 (2.46)
Relative Risk (RR) (95% CI)		0.5479 (0.2219, 1.3533)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1922
Odds Ratio (OR) (95% CI)		0.5365 (0.2109, 1.3650)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1913
Risk Difference (RD) (95% CI)		-0.0203 (-0.0503, 0.0096)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1831
Grade 1/Mild	11 (3.81)	6 (2.11)
Relative Risk (RR) (95% CI)		0.5551 (0.2081, 1.4806)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2396
Odds Ratio (OR) (95% CI)		0.5455 (0.1990, 1.4954)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2388

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0169 (-0.0446, 0.0107)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2305

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	1 (0.35)
Relative Risk (RR) (95% CI)		0.5088 (0.0464, 5.5799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5803
Odds Ratio (OR) (95% CI)		0.5071 (0.0457, 5.6235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5801
Risk Difference (RD) (95% CI)		-0.0034 (-0.0152, 0.0084)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5717
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Blood alkaline phosphatase increased	6 (2.08)	7 (2.46)
Relative Risk (RR) (95% CI)		1.1872 (0.4040, 3.4892)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7551
Odds Ratio (OR) (95% CI)		1.1919 (0.3956, 3.5913)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7550
Risk Difference (RD) (95% CI)		0.0039 (-0.0205, 0.0283)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7549
Grade 1/Mild	2 (0.69)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0069 (-0.0165, 0.0026)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1559

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	7 (2.46)
Relative Risk (RR) (95% CI)		3.5616 (0.7462, 16.9985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1112
Odds Ratio (OR) (95% CI)		3.6264 (0.7469, 17.6078)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1101
Risk Difference (RD) (95% CI)		0.0177 (-0.0027, 0.0381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0887
Grade 3/Severe	2 (0.69)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0069 (-0.0165, 0.0026)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1559

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Blood glucose increased	4 (1.38)	7 (2.46)
Relative Risk (RR) (95% CI)		1.7808 (0.5271, 6.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3529
Odds Ratio (OR) (95% CI)		1.8005 (0.5213, 6.2192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3524
Risk Difference (RD) (95% CI)		0.0108 (-0.0117, 0.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3467
Grade 1/Mild	4 (1.38)	4 (1.41)
Relative Risk (RR) (95% CI)		1.0176 (0.2570, 4.0295)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9802
Odds Ratio (OR) (95% CI)		1.0179 (0.2521, 4.1098)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9802

- MedDRA version 26.1.
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- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0002 (-0.0190, 0.0195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9802

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- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	0	3 (1.06)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0106 (-0.0013, 0.0225)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0816
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Gamma-glutamyltransferase increased	8 (2.77)	6 (2.11)
Relative Risk (RR) (95% CI)		0.7632 (0.2682, 2.1717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6125
Odds Ratio (OR) (95% CI)		0.7581 (0.2597, 2.2132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6124
Risk Difference (RD) (95% CI)		-0.0066 (-0.0318, 0.0187)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6109
Grade 1/Mild	4 (1.38)	2 (0.70)
Relative Risk (RR) (95% CI)		0.5088 (0.0939, 2.7560)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4331
Odds Ratio (OR) (95% CI)		0.5053 (0.0918, 2.7809)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4328

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0068 (-0.0234, 0.0098)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4225

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	2 (0.70)
Relative Risk (RR) (95% CI)		0.6784 (0.1142, 4.0296)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6695
Odds Ratio (OR) (95% CI)		0.6761 (0.1121, 4.0770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6694
Risk Difference (RD) (95% CI)		-0.0033 (-0.0185, 0.0119)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6669
Grade 3/Severe	1 (0.35)	2 (0.70)
Relative Risk (RR) (95% CI)		2.0352 (0.1856, 22.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		2.0426 (0.1842, 22.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0036 (-0.0083, 0.0154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5535

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
SARS-CoV-2 test positive	8 (2.77)	6 (2.11)
Relative Risk (RR) (95% CI)		0.7632 (0.2682, 2.1717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6125
Odds Ratio (OR) (95% CI)		0.7581 (0.2597, 2.2132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6124
Risk Difference (RD) (95% CI)		-0.0066 (-0.0318, 0.0187)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6109
Grade 1/Mild	7 (2.42)	6 (2.11)
Relative Risk (RR) (95% CI)		0.8722 (0.2968, 2.5635)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8037
Odds Ratio (OR) (95% CI)		0.8695 (0.2886, 2.6197)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8037

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0031 (-0.0275, 0.0213)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8034

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [1] Relative risk from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Weight decreased	5 (1.73)	6 (2.11)
Relative Risk (RR) (95% CI)		1.2211 (0.3769, 3.9560)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7391
Odds Ratio (OR) (95% CI)		1.2259 (0.3699, 4.0631)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7390
Risk Difference (RD) (95% CI)		0.0038 (-0.0187, 0.0263)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7388
Grade 1/Mild	4 (1.38)	4 (1.41)
Relative Risk (RR) (95% CI)		1.0176 (0.2570, 4.0295)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9802
Odds Ratio (OR) (95% CI)		1.0179 (0.2521, 4.1098)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9802

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0002 (-0.0190, 0.0195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9802

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	2 (0.70)
Relative Risk (RR) (95% CI)		2.0352 (0.1856, 22.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		2.0426 (0.1842, 22.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607
Risk Difference (RD) (95% CI)		0.0036 (-0.0083, 0.0154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5535
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Blood bilirubin increased	10 (3.46)	5 (1.76)
Relative Risk (RR) (95% CI)		0.5088 (0.1761, 1.4700)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2119
Odds Ratio (OR) (95% CI)		0.5000 (0.1687, 1.4816)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2111
Risk Difference (RD) (95% CI)		-0.0170 (-0.0430, 0.0090)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2008
Grade 1/Mild	5 (1.73)	2 (0.70)
Relative Risk (RR) (95% CI)		0.4070 (0.0796, 2.0809)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2803
Odds Ratio (OR) (95% CI)		0.4028 (0.0775, 2.0935)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2796

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0103 (-0.0282, 0.0076)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2614

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	4 (1.38)	1 (0.35)
Relative Risk (RR) (95% CI)		0.2544 (0.0286, 2.2622)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2195
Odds Ratio (OR) (95% CI)		0.2518 (0.0280, 2.2665)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2186
Risk Difference (RD) (95% CI)		-0.0103 (-0.0254, 0.0048)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1813
Grade 3/Severe	1 (0.35)	2 (0.70)
Relative Risk (RR) (95% CI)		2.0352 (0.1856, 22.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		2.0426 (0.1842, 22.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0036 (-0.0083, 0.0154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5535

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
General disorders and administration site conditions	72 (24.91)	86 (30.28)
Relative Risk (RR) (95% CI)		1.2155 (0.9308, 1.5872)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1518
Odds Ratio (OR) (95% CI)		1.3091 (0.9064, 1.8906)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1510
Risk Difference (RD) (95% CI)		0.0537 (-0.0194, 0.1268)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1500
Grade 1/Mild	54 (18.69)	59 (20.77)
Relative Risk (RR) (95% CI)		1.1118 (0.7987, 1.5478)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5300
Odds Ratio (OR) (95% CI)		1.1412 (0.7559, 1.7228)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5298

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0209 (-0.0443, 0.0861)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5297

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	18 (6.23)	25 (8.80)
Relative Risk (RR) (95% CI)		1.4133 (0.7887, 2.5327)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2451
Odds Ratio (OR) (95% CI)		1.4532 (0.7745, 2.7268)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2444
Risk Difference (RD) (95% CI)		0.0257 (-0.0174, 0.0689)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2423
Grade 3/Severe	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Fatigue	30 (10.38)	33 (11.62)
Relative Risk (RR) (95% CI)		1.1194 (0.7020, 1.7848)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6357
Odds Ratio (OR) (95% CI)		1.1351 (0.6721, 1.9169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6356
Risk Difference (RD) (95% CI)		0.0124 (-0.0389, 0.0636)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6355
Grade 1/Mild	26 (9.00)	26 (9.15)
Relative Risk (RR) (95% CI)		1.0176 (0.6060, 1.7088)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9474
Odds Ratio (OR) (95% CI)		1.0194 (0.5764, 1.8027)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9474

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0016 (-0.0455, 0.0486)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9474

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	4 (1.38)	6 (2.11)
Relative Risk (RR) (95% CI)		1.5264 (0.4354, 5.3518)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5088
Odds Ratio (OR) (95% CI)		1.5378 (0.4293, 5.5081)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5086
Risk Difference (RD) (95% CI)		0.0073 (-0.0142, 0.0288)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5061
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Pyrexia	29 (10.03)	28 (9.86)
Relative Risk (RR) (95% CI)		0.9825 (0.6002, 1.6083)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9441
Odds Ratio (OR) (95% CI)		0.9806 (0.5673, 1.6949)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9441
Risk Difference (RD) (95% CI)		-0.0018 (-0.0508, 0.0473)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9441
Grade 1/Mild	18 (6.23)	18 (6.34)
Relative Risk (RR) (95% CI)		1.0176 (0.5406, 1.9154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9569
Odds Ratio (OR) (95% CI)		1.0188 (0.5188, 2.0007)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9569

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0011 (-0.0386, 0.0408)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9569

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	11 (3.81)	10 (3.52)
Relative Risk (RR) (95% CI)		0.9251 (0.3991, 2.1441)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8559
Odds Ratio (OR) (95% CI)		0.9224 (0.3855, 2.2070)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8559
Risk Difference (RD) (95% CI)		-0.0029 (-0.0336, 0.0279)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8558
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Pain	3 (1.04)	10 (3.52)
Relative Risk (RR) (95% CI)		3.3920 (0.9433, 12.1971)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0614
Odds Ratio (OR) (95% CI)		3.4793 (0.9475, 12.7769)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0603
Risk Difference (RD) (95% CI)		0.0248 (0.0004, 0.0492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0462
Grade 1/Mild	3 (1.04)	9 (3.17)
Relative Risk (RR) (95% CI)		3.0528 (0.8350, 11.1608)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0915
Odds Ratio (OR) (95% CI)		3.1200 (0.8359, 11.6455)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0904

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0213 (-0.0022, 0.0448)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0754

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Influenza like illness	5 (1.73)	7 (2.46)
Relative Risk (RR) (95% CI)		1.4246 (0.4575, 4.4363)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5414
Odds Ratio (OR) (95% CI)		1.4354 (0.4502, 4.5765)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5412
Risk Difference (RD) (95% CI)		0.0073 (-0.0161, 0.0308)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5396
Grade 1/Mild	3 (1.04)	1 (0.35)
Relative Risk (RR) (95% CI)		0.3392 (0.0355, 3.2416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3478
Odds Ratio (OR) (95% CI)		0.3369 (0.0348, 3.2578)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3473

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0069 (-0.0204, 0.0067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3216

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	5 (1.76)
Relative Risk (RR) (95% CI)		2.5440 (0.4976, 13.0055)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2620
Odds Ratio (OR) (95% CI)		2.5717 (0.4948, 13.3651)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2613
Risk Difference (RD) (95% CI)		0.0107 (-0.0074, 0.0287)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2456
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Malaise	4 (1.38)	7 (2.46)
Relative Risk (RR) (95% CI)		1.7808 (0.5271, 6.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3529
Odds Ratio (OR) (95% CI)		1.8005 (0.5213, 6.2192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3524
Risk Difference (RD) (95% CI)		0.0108 (-0.0117, 0.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3467
Grade 1/Mild	4 (1.38)	7 (2.46)
Relative Risk (RR) (95% CI)		1.7808 (0.5271, 6.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3529
Odds Ratio (OR) (95% CI)		1.8005 (0.5213, 6.2192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3524

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0108 (-0.0117, 0.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3467

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Nervous system disorders	64 (22.15)	72 (25.35)
Relative Risk (RR) (95% CI)		1.1448 (0.8530, 1.5364)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3676
Odds Ratio (OR) (95% CI)		1.1940 (0.8121, 1.7555)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3673
Risk Difference (RD) (95% CI)		0.0321 (-0.0376, 0.1017)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3669
Grade 1/Mild	40 (13.84)	47 (16.55)
Relative Risk (RR) (95% CI)		1.1957 (0.8107, 1.7634)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3673
Odds Ratio (OR) (95% CI)		1.2345 (0.7812, 1.9509)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3669

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0271 (-0.0317, 0.0858)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3663

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	20 (6.92)	21 (7.39)
Relative Risk (RR) (95% CI)		1.0685 (0.5923, 1.9277)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8258
Odds Ratio (OR) (95% CI)		1.0740 (0.5688, 2.0276)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8258
Risk Difference (RD) (95% CI)		0.0047 (-0.0375, 0.0470)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8259
Grade 3/Severe	4 (1.38)	4 (1.41)
Relative Risk (RR) (95% CI)		1.0176 (0.2570, 4.0295)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9802
Odds Ratio (OR) (95% CI)		1.0179 (0.2521, 4.1098)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9802

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0002 (-0.0190, 0.0195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9802

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Headache	41 (14.19)	51 (17.96)
Relative Risk (RR) (95% CI)		1.2658 (0.8682, 1.8456)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2205
Odds Ratio (OR) (95% CI)		1.3240 (0.8456, 2.0729)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2199
Risk Difference (RD) (95% CI)		0.0377 (-0.0224, 0.0978)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2187
Grade 1/Mild	27 (9.34)	37 (13.03)
Relative Risk (RR) (95% CI)		1.3945 (0.8731, 2.2273)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1640
Odds Ratio (OR) (95% CI)		1.4536 (0.8593, 2.4588)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1631

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0369 (-0.0147, 0.0884)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1612

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	12 (4.15)	14 (4.93)
Relative Risk (RR) (95% CI)		1.1872 (0.5589, 2.5220)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6553
Odds Ratio (OR) (95% CI)		1.1969 (0.5437, 2.6348)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6553
Risk Difference (RD) (95% CI)		0.0078 (-0.0263, 0.0419)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6550
Grade 3/Severe	2 (0.69)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0069 (-0.0165, 0.0026)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1559

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Dizziness	13 (4.50)	9 (3.17)
Relative Risk (RR) (95% CI)		0.7045 (0.3060, 1.6221)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4104
Odds Ratio (OR) (95% CI)		0.6948 (0.2922, 1.6521)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4100
Risk Difference (RD) (95% CI)		-0.0133 (-0.0447, 0.0181)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4067
Grade 1/Mild	9 (3.11)	8 (2.82)
Relative Risk (RR) (95% CI)		0.9045 (0.3540, 2.3114)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8340
Odds Ratio (OR) (95% CI)		0.9018 (0.3430, 2.3712)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8340

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0030 (-0.0307, 0.0248)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8338

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	4 (1.38)	1 (0.35)
Relative Risk (RR) (95% CI)		0.2544 (0.0286, 2.2622)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2195
Odds Ratio (OR) (95% CI)		0.2518 (0.0280, 2.2665)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2186
Risk Difference (RD) (95% CI)		-0.0103 (-0.0254, 0.0048)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1813
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Migraine	5 (1.73)	5 (1.76)
Relative Risk (RR) (95% CI)		1.0176 (0.2978, 3.4770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9778
Odds Ratio (OR) (95% CI)		1.0179 (0.2915, 3.5549)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9778
Risk Difference (RD) (95% CI)		0.0003 (-0.0211, 0.0218)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9778
Grade 1/Mild	2 (0.69)	2 (0.70)
Relative Risk (RR) (95% CI)		1.0176 (0.1443, 7.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9860
Odds Ratio (OR) (95% CI)		1.0177 (0.1424, 7.2748)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9860

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0001 (-0.0135, 0.0138)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9860

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	1 (0.35)
Relative Risk (RR) (95% CI)		0.3392 (0.0355, 3.2416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3478
Odds Ratio (OR) (95% CI)		0.3369 (0.0348, 3.2578)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3473
Risk Difference (RD) (95% CI)		-0.0069 (-0.0204, 0.0067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3216
Grade 3/Severe	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Skin and subcutaneous tissue disorders	52 (17.99)	68 (23.94)
Relative Risk (RR) (95% CI)		1.3307 (0.9646, 1.8358)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0818
Odds Ratio (OR) (95% CI)		1.4348 (0.9566, 2.1521)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0809
Risk Difference (RD) (95% CI)		0.0595 (-0.0070, 0.1260)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0795
Grade 1/Mild	38 (13.15)	45 (15.85)
Relative Risk (RR) (95% CI)		1.2051 (0.8081, 1.7969)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3602
Odds Ratio (OR) (95% CI)		1.2437 (0.7798, 1.9834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3598

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0270 (-0.0307, 0.0846)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3592

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	14 (4.84)	22 (7.75)
Relative Risk (RR) (95% CI)		1.5991 (0.8350, 3.0624)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1568
Odds Ratio (OR) (95% CI)		1.6494 (0.8264, 3.2921)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1559
Risk Difference (RD) (95% CI)		0.0290 (-0.0107, 0.0688)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1523
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Rash	13 (4.50)	25 (8.80)
Relative Risk (RR) (95% CI)		1.9569 (1.0217, 3.7481)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0429
Odds Ratio (OR) (95% CI)		2.0493 (1.0265, 4.0911)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0419
Risk Difference (RD) (95% CI)		0.0430 (0.0023, 0.0838)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0382
Grade 1/Mild	5 (1.73)	17 (5.99)
Relative Risk (RR) (95% CI)		3.4599 (1.2939, 9.2518)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0134
Odds Ratio (OR) (95% CI)		3.6165 (1.3158, 9.9396)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0127

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0426 (0.0111, 0.0740)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0079

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	8 (2.77)	7 (2.46)
Relative Risk (RR) (95% CI)		0.8904 (0.3272, 2.4230)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8202
Odds Ratio (OR) (95% CI)		0.8876 (0.3176, 2.4810)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8202
Risk Difference (RD) (95% CI)		-0.0030 (-0.0292, 0.0231)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8200
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [1] Relative risk from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Acne	12 (4.15)	11 (3.87)
Relative Risk (RR) (95% CI)		0.9328 (0.4185, 2.0793)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8649
Odds Ratio (OR) (95% CI)		0.9301 (0.4035, 2.1438)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8649
Risk Difference (RD) (95% CI)		-0.0028 (-0.0349, 0.0293)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8649
Grade 1/Mild	12 (4.15)	8 (2.82)
Relative Risk (RR) (95% CI)		0.6784 (0.2815, 1.6347)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3872
Odds Ratio (OR) (95% CI)		0.6691 (0.2693, 1.6622)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3868

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0134 (-0.0433, 0.0166)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3828

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	0	3 (1.06)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0106 (-0.0013, 0.0225)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0816
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Pruritus	6 (2.08)	9 (3.17)
Relative Risk (RR) (95% CI)		1.5264 (0.5505, 4.2327)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4164
Odds Ratio (OR) (95% CI)		1.5436 (0.5422, 4.3946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4160
Risk Difference (RD) (95% CI)		0.0109 (-0.0152, 0.0371)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4132
Grade 1/Mild	4 (1.38)	6 (2.11)
Relative Risk (RR) (95% CI)		1.5264 (0.4354, 5.3518)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5088
Odds Ratio (OR) (95% CI)		1.5378 (0.4293, 5.5081)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5086

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0073 (-0.0142, 0.0288)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5061

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	3 (1.06)
Relative Risk (RR) (95% CI)		1.5264 (0.2570, 9.0666)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6418
Odds Ratio (OR) (95% CI)		1.5320 (0.2541, 9.2381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6417
Risk Difference (RD) (95% CI)		0.0036 (-0.0116, 0.0189)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6398
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [1] Relative risk from 2x2 table.
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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Alopecia	6 (2.08)	5 (1.76)
Relative Risk (RR) (95% CI)		0.8480 (0.2618, 2.7472)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7834
Odds Ratio (OR) (95% CI)		0.8453 (0.2550, 2.8016)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7834
Risk Difference (RD) (95% CI)		-0.0032 (-0.0256, 0.0193)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7830
Grade 1/Mild	6 (2.08)	3 (1.06)
Relative Risk (RR) (95% CI)		0.5088 (0.1285, 2.0148)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3359
Odds Ratio (OR) (95% CI)		0.5036 (0.1247, 2.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3353

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0102 (-0.0305, 0.0101)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3245

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Musculoskeletal and connective tissue disorders	71 (24.57)	55 (19.37)
Relative Risk (RR) (95% CI)		0.7883 (0.5772, 1.0766)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1346
Odds Ratio (OR) (95% CI)		0.7374 (0.4953, 1.0978)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1336
Risk Difference (RD) (95% CI)		-0.0520 (-0.1197, 0.0156)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1318
Grade 1/Mild	42 (14.53)	36 (12.68)
Relative Risk (RR) (95% CI)		0.8722 (0.5766, 1.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5175
Odds Ratio (OR) (95% CI)		0.8537 (0.5289, 1.3779)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5172

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0186 (-0.0747, 0.0375)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5166

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	29 (10.03)	18 (6.34)
Relative Risk (RR) (95% CI)		0.6316 (0.3590, 1.1111)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1109
Odds Ratio (OR) (95% CI)		0.6067 (0.3288, 1.1193)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1098
Risk Difference (RD) (95% CI)		-0.0370 (-0.0817, 0.0078)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1055
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Back pain	15 (5.19)	16 (5.63)
Relative Risk (RR) (95% CI)		1.0854 (0.5471, 2.1535)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8145
Odds Ratio (OR) (95% CI)		1.0905 (0.5286, 2.2500)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8145
Risk Difference (RD) (95% CI)		0.0044 (-0.0326, 0.0415)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8145
Grade 1/Mild	9 (3.11)	10 (3.52)
Relative Risk (RR) (95% CI)		1.1307 (0.4664, 2.7410)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7858
Odds Ratio (OR) (95% CI)		1.1354 (0.4544, 2.8373)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7857

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0041 (-0.0253, 0.0334)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7857

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	6 (2.08)	6 (2.11)
Relative Risk (RR) (95% CI)		1.0176 (0.3321, 3.1178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9756
Odds Ratio (OR) (95% CI)		1.0180 (0.3244, 3.1946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9756
Risk Difference (RD) (95% CI)		0.0004 (-0.0231, 0.0238)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9756
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- [1] Relative risk from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Arthralgia	25 (8.65)	14 (4.93)
Relative Risk (RR) (95% CI)		0.5699 (0.3025, 1.0736)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0818
Odds Ratio (OR) (95% CI)		0.5476 (0.2785, 1.0764)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0807
Risk Difference (RD) (95% CI)		-0.0372 (-0.0782, 0.0038)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0756
Grade 1/Mild	18 (6.23)	10 (3.52)
Relative Risk (RR) (95% CI)		0.5653 (0.2656, 1.2034)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1390
Odds Ratio (OR) (95% CI)		0.5495 (0.2491, 1.2120)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1379

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0271 (-0.0622, 0.0081)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1312

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	7 (2.42)	3 (1.06)
Relative Risk (RR) (95% CI)		0.4361 (0.1139, 1.6698)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2257
Odds Ratio (OR) (95% CI)		0.4301 (0.1101, 1.6800)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2249
Risk Difference (RD) (95% CI)		-0.0137 (-0.0350, 0.0077)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2098
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Myalgia	7 (2.42)	10 (3.52)
Relative Risk (RR) (95% CI)		1.4537 (0.5611, 3.7660)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4411
Odds Ratio (OR) (95% CI)		1.4703 (0.5518, 3.9178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4408
Risk Difference (RD) (95% CI)		0.0110 (-0.0168, 0.0388)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4387
Grade 1/Mild	6 (2.08)	9 (3.17)
Relative Risk (RR) (95% CI)		1.5264 (0.5505, 4.2327)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4164
Odds Ratio (OR) (95% CI)		1.5436 (0.5422, 4.3946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4160

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0109 (-0.0152, 0.0371)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4132

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- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Pain in extremity	7 (2.42)	6 (2.11)
Relative Risk (RR) (95% CI)		0.8722 (0.2968, 2.5635)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8037
Odds Ratio (OR) (95% CI)		0.8695 (0.2886, 2.6197)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8037
Risk Difference (RD) (95% CI)		-0.0031 (-0.0275, 0.0213)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8034
Grade 1/Mild	4 (1.38)	5 (1.76)
Relative Risk (RR) (95% CI)		1.2720 (0.3451, 4.6886)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7177
Odds Ratio (OR) (95% CI)		1.2769 (0.3394, 4.8044)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7177

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0038 (-0.0166, 0.0241)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7173

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- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	1 (0.35)
Relative Risk (RR) (95% CI)		0.3392 (0.0355, 3.2416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3478
Odds Ratio (OR) (95% CI)		0.3369 (0.0348, 3.2578)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3473
Risk Difference (RD) (95% CI)		-0.0069 (-0.0204, 0.0067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3216
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Musculoskeletal chest pain	7 (2.42)	4 (1.41)
Relative Risk (RR) (95% CI)		0.5815 (0.1721, 1.9647)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3828
Odds Ratio (OR) (95% CI)		0.5755 (0.1666, 1.9878)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3823
Risk Difference (RD) (95% CI)		-0.0101 (-0.0325, 0.0123)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3752
Grade 1/Mild	6 (2.08)	4 (1.41)
Relative Risk (RR) (95% CI)		0.6784 (0.1935, 2.3786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5444
Odds Ratio (OR) (95% CI)		0.6738 (0.1881, 2.4135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5442

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0067 (-0.0281, 0.0147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5409

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Injury, poisoning and procedural complications	53 (18.34)	46 (16.20)
Relative Risk (RR) (95% CI)		0.8832 (0.6166, 1.2652)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4982
Odds Ratio (OR) (95% CI)		0.8606 (0.5576, 1.3284)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4980
Risk Difference (RD) (95% CI)		-0.0214 (-0.0833, 0.0404)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4974
Grade 1/Mild	31 (10.73)	27 (9.51)
Relative Risk (RR) (95% CI)		0.8863 (0.5434, 1.4457)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6287
Odds Ratio (OR) (95% CI)		0.8744 (0.5075, 1.5065)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6286

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0122 (-0.0616, 0.0372)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6282

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	20 (6.92)	18 (6.34)
Relative Risk (RR) (95% CI)		0.9158 (0.4950, 1.6946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7795
Odds Ratio (OR) (95% CI)		0.9102 (0.4709, 1.7591)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7795
Risk Difference (RD) (95% CI)		-0.0058 (-0.0466, 0.0349)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7793
Grade 3/Severe	2 (0.69)	1 (0.35)
Relative Risk (RR) (95% CI)		0.5088 (0.0464, 5.5799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5803
Odds Ratio (OR) (95% CI)		0.5071 (0.0457, 5.6235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5801

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0034 (-0.0152, 0.0084)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5717

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Psychiatric disorders	36 (12.46)	41 (14.44)
Relative Risk (RR) (95% CI)		1.1589 (0.7640, 1.7579)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4877
Odds Ratio (OR) (95% CI)		1.1858 (0.7330, 1.9183)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4875
Risk Difference (RD) (95% CI)		0.0198 (-0.0361, 0.0757)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4873
Grade 1/Mild	17 (5.88)	23 (8.10)
Relative Risk (RR) (95% CI)		1.3768 (0.7517, 2.5215)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3004
Odds Ratio (OR) (95% CI)		1.4100 (0.7364, 2.6994)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2998

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0222 (-0.0196, 0.0639)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2981

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	17 (5.88)	16 (5.63)
Relative Risk (RR) (95% CI)		0.9577 (0.4937, 1.8581)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8984
Odds Ratio (OR) (95% CI)		0.9552 (0.4728, 1.9298)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8984
Risk Difference (RD) (95% CI)		-0.0025 (-0.0406, 0.0357)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8984
Grade 3/Severe	2 (0.69)	2 (0.70)
Relative Risk (RR) (95% CI)		1.0176 (0.1443, 7.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9860
Odds Ratio (OR) (95% CI)		1.0177 (0.1424, 7.2748)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9860

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0001 (-0.0135, 0.0138)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9860

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Anxiety	6 (2.08)	16 (5.63)
Relative Risk (RR) (95% CI)		2.7136 (1.0773, 6.8356)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0342
Odds Ratio (OR) (95% CI)		2.8159 (1.0858, 7.3032)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0332
Risk Difference (RD) (95% CI)		0.0356 (0.0041, 0.0670)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0266
Grade 1/Mild	3 (1.04)	9 (3.17)
Relative Risk (RR) (95% CI)		3.0528 (0.8350, 11.1608)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0915
Odds Ratio (OR) (95% CI)		3.1200 (0.8359, 11.6455)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0904

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0213 (-0.0022, 0.0448)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0754

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	6 (2.11)
Relative Risk (RR) (95% CI)		2.0352 (0.5140, 8.0590)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3115
Odds Ratio (OR) (95% CI)		2.0576 (0.5096, 8.3080)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3110
Risk Difference (RD) (95% CI)		0.0107 (-0.0097, 0.0311)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3019
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Insomnia	14 (4.84)	11 (3.87)
Relative Risk (RR) (95% CI)		0.7995 (0.3693, 1.7312)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5703
Odds Ratio (OR) (95% CI)		0.7915 (0.3531, 1.7743)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5702
Risk Difference (RD) (95% CI)		-0.0097 (-0.0431, 0.0237)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5689
Grade 1/Mild	7 (2.42)	6 (2.11)
Relative Risk (RR) (95% CI)		0.8722 (0.2968, 2.5635)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8037
Odds Ratio (OR) (95% CI)		0.8695 (0.2886, 2.6197)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8037

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0031 (-0.0275, 0.0213)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8034

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	7 (2.42)	4 (1.41)
Relative Risk (RR) (95% CI)		0.5815 (0.1721, 1.9647)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3828
Odds Ratio (OR) (95% CI)		0.5755 (0.1666, 1.9878)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3823
Risk Difference (RD) (95% CI)		-0.0101 (-0.0325, 0.0123)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3752
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- [1] Relative risk from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Depression	3 (1.04)	10 (3.52)
Relative Risk (RR) (95% CI)		3.3920 (0.9433, 12.1971)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0614
Odds Ratio (OR) (95% CI)		3.4793 (0.9475, 12.7769)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0603
Risk Difference (RD) (95% CI)		0.0248 (0.0004, 0.0492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0462
Grade 1/Mild	1 (0.35)	6 (2.11)
Relative Risk (RR) (95% CI)		6.1056 (0.7397, 50.3940)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0929
Odds Ratio (OR) (95% CI)		6.2158 (0.7436, 51.9617)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0917

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0177 (-0.0004, 0.0357)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0550

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	2 (0.70)
Relative Risk (RR) (95% CI)		1.0176 (0.1443, 7.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9860
Odds Ratio (OR) (95% CI)		1.0177 (0.1424, 7.2748)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9860
Risk Difference (RD) (95% CI)		0.0001 (-0.0135, 0.0138)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9860
Grade 3/Severe	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Metabolism and nutrition disorders	25 (8.65)	25 (8.80)
Relative Risk (RR) (95% CI)		1.0176 (0.5992, 1.7282)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9485
Odds Ratio (OR) (95% CI)		1.0193 (0.5706, 1.8210)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9485
Risk Difference (RD) (95% CI)		0.0015 (-0.0447, 0.0477)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9485
Grade 1/Mild	18 (6.23)	18 (6.34)
Relative Risk (RR) (95% CI)		1.0176 (0.5406, 1.9154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9569
Odds Ratio (OR) (95% CI)		1.0188 (0.5188, 2.0007)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9569

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0011 (-0.0386, 0.0408)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9569

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	6 (2.08)	7 (2.46)
Relative Risk (RR) (95% CI)		1.1872 (0.4040, 3.4892)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7551
Odds Ratio (OR) (95% CI)		1.1919 (0.3956, 3.5913)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7550
Risk Difference (RD) (95% CI)		0.0039 (-0.0205, 0.0283)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7549
Grade 3/Severe	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Decreased appetite	8 (2.77)	3 (1.06)
Relative Risk (RR) (95% CI)		0.3816 (0.1023, 1.4239)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1516
Odds Ratio (OR) (95% CI)		0.3750 (0.0985, 1.4281)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1505
Risk Difference (RD) (95% CI)		-0.0171 (-0.0395, 0.0052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1332
Grade 1/Mild	8 (2.77)	3 (1.06)
Relative Risk (RR) (95% CI)		0.3816 (0.1023, 1.4239)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1516
Odds Ratio (OR) (95% CI)		0.3750 (0.0985, 1.4281)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1505

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- [3] Risk difference estimate from 2x2 table.
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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0171 (-0.0395, 0.0052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1332

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- [1] Relative risk from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Eye disorders	18 (6.23)	17 (5.99)
Relative Risk (RR) (95% CI)		0.9611 (0.5056, 1.8269)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9036
Odds Ratio (OR) (95% CI)		0.9586 (0.4837, 1.8999)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9036
Risk Difference (RD) (95% CI)		-0.0024 (-0.0416, 0.0368)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9035
Grade 1/Mild	15 (5.19)	12 (4.23)
Relative Risk (RR) (95% CI)		0.8141 (0.3879, 1.7083)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5865
Odds Ratio (OR) (95% CI)		0.8059 (0.3704, 1.7535)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5864

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- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0096 (-0.0443, 0.0250)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5853

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	5 (1.76)
Relative Risk (RR) (95% CI)		1.6960 (0.4091, 7.0303)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4665
Odds Ratio (OR) (95% CI)		1.7085 (0.4045, 7.2169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4663
Risk Difference (RD) (95% CI)		0.0072 (-0.0120, 0.0265)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4619
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Renal and urinary disorders	15 (5.19)	10 (3.52)
Relative Risk (RR) (95% CI)		0.6784 (0.3100, 1.4847)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3316
Odds Ratio (OR) (95% CI)		0.6667 (0.2944, 1.5099)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3310
Risk Difference (RD) (95% CI)		-0.0167 (-0.0501, 0.0167)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3269
Grade 1/Mild	7 (2.42)	5 (1.76)
Relative Risk (RR) (95% CI)		0.7269 (0.2334, 2.2634)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5820
Odds Ratio (OR) (95% CI)		0.7220 (0.2264, 2.3019)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5819

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0066 (-0.0300, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5797

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- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	7 (2.42)	4 (1.41)
Relative Risk (RR) (95% CI)		0.5815 (0.1721, 1.9647)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3828
Odds Ratio (OR) (95% CI)		0.5755 (0.1666, 1.9878)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3823
Risk Difference (RD) (95% CI)		-0.0101 (-0.0325, 0.0123)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3752
Grade 3/Severe	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Nephrolithiasis	6 (2.08)	4 (1.41)
Relative Risk (RR) (95% CI)		0.6784 (0.1935, 2.3786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5444
Odds Ratio (OR) (95% CI)		0.6738 (0.1881, 2.4135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5442
Risk Difference (RD) (95% CI)		-0.0067 (-0.0281, 0.0147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5409
Grade 1/Mild	2 (0.69)	1 (0.35)
Relative Risk (RR) (95% CI)		0.5088 (0.0464, 5.5799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5803
Odds Ratio (OR) (95% CI)		0.5071 (0.0457, 5.6235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5801

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0034 (-0.0152, 0.0084)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5717

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	2 (0.70)
Relative Risk (RR) (95% CI)		0.6784 (0.1142, 4.0296)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6695
Odds Ratio (OR) (95% CI)		0.6761 (0.1121, 4.0770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6694
Risk Difference (RD) (95% CI)		-0.0033 (-0.0185, 0.0119)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6669
Grade 3/Severe	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Reproductive system and breast disorders	19 (6.57)	10 (3.52)
Relative Risk (RR) (95% CI)		0.5356 (0.2535, 1.1316)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1018
Odds Ratio (OR) (95% CI)		0.5186 (0.2368, 1.1359)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1007
Risk Difference (RD) (95% CI)		-0.0305 (-0.0663, 0.0052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0939
Grade 1/Mild	10 (3.46)	4 (1.41)
Relative Risk (RR) (95% CI)		0.4070 (0.1292, 1.2828)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1249
Odds Ratio (OR) (95% CI)		0.3986 (0.1235, 1.2859)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1238

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0205 (-0.0457, 0.0046)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1096

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	8 (2.77)	6 (2.11)
Relative Risk (RR) (95% CI)		0.7632 (0.2682, 2.1717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6125
Odds Ratio (OR) (95% CI)		0.7581 (0.2597, 2.2132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6124
Risk Difference (RD) (95% CI)		-0.0066 (-0.0318, 0.0187)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6109
Grade 3/Severe	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Ear and labyrinth disorders	11 (3.81)	9 (3.17)
Relative Risk (RR) (95% CI)		0.8326 (0.3504, 1.9786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6782
Odds Ratio (OR) (95% CI)		0.8271 (0.3374, 2.0274)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6782
Risk Difference (RD) (95% CI)		-0.0064 (-0.0364, 0.0237)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6775
Grade 1/Mild	10 (3.46)	9 (3.17)
Relative Risk (RR) (95% CI)		0.9158 (0.3778, 2.2202)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8457
Odds Ratio (OR) (95% CI)		0.9131 (0.3654, 2.2816)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8457

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0029 (-0.0322, 0.0264)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8456

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Congenital, familial and genetic disorders	5 (1.73)	8 (2.82)
Relative Risk (RR) (95% CI)		1.6282 (0.5391, 4.9172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3874
Odds Ratio (OR) (95% CI)		1.6464 (0.5321, 5.0944)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3870
Risk Difference (RD) (95% CI)		0.0109 (-0.0136, 0.0353)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3830
Grade 1/Mild	5 (1.73)	6 (2.11)
Relative Risk (RR) (95% CI)		1.2211 (0.3769, 3.9560)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7391
Odds Ratio (OR) (95% CI)		1.2259 (0.3699, 4.0631)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7390

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0038 (-0.0187, 0.0263)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7388

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Immune system disorders	8 (2.77)	8 (2.82)
Relative Risk (RR) (95% CI)		1.0176 (0.3872, 2.6742)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9718
Odds Ratio (OR) (95% CI)		1.0181 (0.3768, 2.7509)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9718
Risk Difference (RD) (95% CI)		0.0005 (-0.0265, 0.0275)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9718
Grade 1/Mild	6 (2.08)	6 (2.11)
Relative Risk (RR) (95% CI)		1.0176 (0.3321, 3.1178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9756
Odds Ratio (OR) (95% CI)		1.0180 (0.3244, 3.1946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9756

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0004 (-0.0231, 0.0238)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9756

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	1 (0.35)
Relative Risk (RR) (95% CI)		0.5088 (0.0464, 5.5799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5803
Odds Ratio (OR) (95% CI)		0.5071 (0.0457, 5.6235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5801
Risk Difference (RD) (95% CI)		-0.0034 (-0.0152, 0.0084)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5717
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Seasonal allergy	6 (2.08)	7 (2.46)
Relative Risk (RR) (95% CI)		1.1872 (0.4040, 3.4892)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7551
Odds Ratio (OR) (95% CI)		1.1919 (0.3956, 3.5913)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7550
Risk Difference (RD) (95% CI)		0.0039 (-0.0205, 0.0283)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7549
Grade 1/Mild	5 (1.73)	5 (1.76)
Relative Risk (RR) (95% CI)		1.0176 (0.2978, 3.4770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9778
Odds Ratio (OR) (95% CI)		1.0179 (0.2915, 3.5549)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9778

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0003 (-0.0211, 0.0218)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9778

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Cardiac disorders	4 (1.38)	7 (2.46)
Relative Risk (RR) (95% CI)		1.7808 (0.5271, 6.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3529
Odds Ratio (OR) (95% CI)		1.8005 (0.5213, 6.2192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3524
Risk Difference (RD) (95% CI)		0.0108 (-0.0117, 0.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3467
Grade 1/Mild	4 (1.38)	5 (1.76)
Relative Risk (RR) (95% CI)		1.2720 (0.3451, 4.6886)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7177
Odds Ratio (OR) (95% CI)		1.2769 (0.3394, 4.8044)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7177

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0038 (-0.0166, 0.0241)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7173

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [2] Odds ratio from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Vascular disorders	9 (3.11)	5 (1.76)
Relative Risk (RR) (95% CI)		0.5653 (0.1918, 1.6662)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3010
Odds Ratio (OR) (95% CI)		0.5575 (0.1845, 1.6846)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3004
Risk Difference (RD) (95% CI)		-0.0135 (-0.0387, 0.0117)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2924
Grade 1/Mild	6 (2.08)	5 (1.76)
Relative Risk (RR) (95% CI)		0.8480 (0.2618, 2.7472)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7834
Odds Ratio (OR) (95% CI)		0.8453 (0.2550, 2.8016)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7834

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0032 (-0.0256, 0.0193)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7830

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0104 (-0.0221, 0.0013)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0817
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Hepatobiliary disorders	9 (3.11)	4 (1.41)
Relative Risk (RR) (95% CI)		0.4523 (0.1409, 1.4519)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1824
Odds Ratio (OR) (95% CI)		0.4444 (0.1353, 1.4600)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1814
Risk Difference (RD) (95% CI)		-0.0171 (-0.0413, 0.0072)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1683
Grade 1/Mild	4 (1.38)	2 (0.70)
Relative Risk (RR) (95% CI)		0.5088 (0.0939, 2.7560)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4331
Odds Ratio (OR) (95% CI)		0.5053 (0.0918, 2.7809)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4328

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0068 (-0.0234, 0.0098)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4225

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	2 (0.70)
Relative Risk (RR) (95% CI)		2.0352 (0.1856, 22.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		2.0426 (0.1842, 22.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607
Risk Difference (RD) (95% CI)		0.0036 (-0.0083, 0.0154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5535
Grade 3/Severe	4 (1.38)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0138 (-0.0273, -0.0004)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0440

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with any Grade 3/4/5 TEAEs	29 (10.03)	24 (8.45)
Relative Risk (RR) (95% CI)		0.8422 (0.5030, 1.4101)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5136
Odds Ratio (OR) (95% CI)		0.8276 (0.4692, 1.4598)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5134
Risk Difference (RD) (95% CI)		-0.0158 (-0.0632, 0.0316)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5125
Infections and infestations	6 (2.08)	5 (1.76)
Relative Risk (RR) (95% CI)		0.8480 (0.2618, 2.7472)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7834
Odds Ratio (OR) (95% CI)		0.8453 (0.2550, 2.8016)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7834

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0032 (-0.0256, 0.0193)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7830

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Investigations	5 (1.73)	5 (1.76)
Relative Risk (RR) (95% CI)		1.0176 (0.2978, 3.4770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9778
Odds Ratio (OR) (95% CI)		1.0179 (0.2915, 3.5549)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9778
Risk Difference (RD) (95% CI)		0.0003 (-0.0211, 0.0218)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9778

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- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.3
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with any serious TEAEs	33 (11.42)	23 (8.10)
Relative Risk (RR) (95% CI)		0.7092 (0.4274, 1.1770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1838
Odds Ratio (OR) (95% CI)		0.6836 (0.3906, 1.1963)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1828
Risk Difference (RD) (95% CI)		-0.0332 (-0.0817, 0.0153)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1796
Infections and infestations	12 (4.15)	9 (3.17)
Relative Risk (RR) (95% CI)		0.7632 (0.3267, 1.7831)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5325
Odds Ratio (OR) (95% CI)		0.7555 (0.3133, 1.8217)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5323

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.3
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0098 (-0.0406, 0.0209)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5305

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.3
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Gastrointestinal disorders	7 (2.42)	3 (1.06)
Relative Risk (RR) (95% CI)		0.4361 (0.1139, 1.6698)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2257
Odds Ratio (OR) (95% CI)		0.4301 (0.1101, 1.6800)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2249
Risk Difference (RD) (95% CI)		-0.0137 (-0.0350, 0.0077)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2098

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- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with any TEAEs leading to treatment discontinuation	9 (3.11)	14 (4.93)
Relative Risk (RR) (95% CI)		1.5829 (0.6963, 3.5985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2730
Odds Ratio (OR) (95% CI)		1.6132 (0.6868, 3.7890)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2724
Risk Difference (RD) (95% CI)		0.0182 (-0.0140, 0.0503)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2687
Investigations	3 (1.04)	7 (2.46)
Relative Risk (RR) (95% CI)		2.3744 (0.6201, 9.0912)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2068
Odds Ratio (OR) (95% CI)		2.4091 (0.6168, 9.4105)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2059

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0143 (-0.0072, 0.0358)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1931

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Alanine aminotransferase increased	2 (0.69)	6 (2.11)
Relative Risk (RR) (95% CI)		3.0528 (0.6214, 14.9988)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1694
Odds Ratio (OR) (95% CI)		3.0971 (0.6198, 15.4754)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1684
Risk Difference (RD) (95% CI)		0.0142 (-0.0051, 0.0335)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1483
Aspartate aminotransferase increased	2 (0.69)	5 (1.76)
Relative Risk (RR) (95% CI)		2.5440 (0.4976, 13.0055)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2620
Odds Ratio (OR) (95% CI)		2.5717 (0.4948, 13.3651)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2613
Risk Difference (RD) (95% CI)		0.0107 (-0.0074, 0.0287)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2456

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Blood bilirubin increased	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558
Blood bilirubin unconjugated increased	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558

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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Blood alkaline phosphatase increased	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901
Blood creatine phosphokinase increased	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Gamma-glutamyltransferase increased	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901
Sputum abnormal	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Pulmonary function test decreased	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
General disorders and administration site conditions	1 (0.35)	3 (1.06)
Relative Risk (RR) (95% CI)		3.0528 (0.3194, 29.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3325
Odds Ratio (OR) (95% CI)		3.0747 (0.3179, 29.7357)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3320
Risk Difference (RD) (95% CI)		0.0071 (-0.0066, 0.0208)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3089

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Fatigue	1 (0.35)	3 (1.06)
Relative Risk (RR) (95% CI)		3.0528 (0.3194, 29.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3325
Odds Ratio (OR) (95% CI)		3.0747 (0.3179, 29.7357)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3320
Risk Difference (RD) (95% CI)		0.0071 (-0.0066, 0.0208)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3089
Respiratory, thoracic and mediastinal disorders	1 (0.35)	3 (1.06)
Relative Risk (RR) (95% CI)		3.0528 (0.3194, 29.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3325
Odds Ratio (OR) (95% CI)		3.0747 (0.3179, 29.7357)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3320
Risk Difference (RD) (95% CI)		0.0071 (-0.0066, 0.0208)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3089

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Cough	1 (0.35)	2 (0.70)
Relative Risk (RR) (95% CI)		2.0352 (0.1856, 22.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		2.0426 (0.1842, 22.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607
Risk Difference (RD) (95% CI)		0.0036 (-0.0083, 0.0154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5535
Dysphonia	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Sputum discoloured	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Sputum increased	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Nervous system disorders	1 (0.35)	2 (0.70)
Relative Risk (RR) (95% CI)		2.0352 (0.1856, 22.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		2.0426 (0.1842, 22.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607
Risk Difference (RD) (95% CI)		0.0036 (-0.0083, 0.0154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5535
Amnesia	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Lethargy	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Hyperresponsive to stimuli	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Psychiatric disorders	1 (0.35)	2 (0.70)
Relative Risk (RR) (95% CI)		2.0352 (0.1856, 22.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		2.0426 (0.1842, 22.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607
Risk Difference (RD) (95% CI)		0.0036 (-0.0083, 0.0154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5535
Agitation	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Anxiety	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Depression	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Insomnia	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Mental fatigue	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Stress	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Reproductive system and breast disorders	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Heavy menstrual bleeding	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Gastrointestinal disorders	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Distal intestinal obstruction syndrome	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Hepatobiliary disorders	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Cholangitis	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Metabolism and nutrition disorders	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Malnutrition	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.5
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events - Total and by Severity
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	22 (7.61)	27 (9.51)
Relative Risk (RR) (95% CI)		1.2489 (0.7288, 2.1400)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4186
Odds Ratio (OR) (95% CI)		1.2750 (0.7079, 2.2965)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4183
Risk Difference (RD) (95% CI)		0.0189 (-0.0269, 0.0648)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4176
Subjects with non-severe events (Maximum Grade 1/2)	22 (7.61)	23 (8.10)
Relative Risk (RR) (95% CI)		1.0639 (0.6070, 1.8645)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8288
Odds Ratio (OR) (95% CI)		1.0695 (0.5818, 1.9661)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8288
Risk Difference (RD) (95% CI)		0.0049 (-0.0392, 0.0489)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8288

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.5
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events - Total and by Severity
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with severe events (Maximum Grade 3/4/5)	0	4 (1.41)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0141 (0.0004, 0.0278)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0440
Subjects with serious events	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.6
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events - Total and by Severity
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	17 (5.88)	25 (8.80)
Relative Risk (RR) (95% CI)		1.4965 (0.8262, 2.7104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1835
Odds Ratio (OR) (95% CI)		1.5444 (0.8150, 2.9266)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1826
Risk Difference (RD) (95% CI)		0.0292 (-0.0135, 0.0719)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1799
Subjects with non-severe events (Maximum Grade 1/2)	16 (5.54)	24 (8.45)
Relative Risk (RR) (95% CI)		1.5264 (0.8285, 2.8121)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1749
Odds Ratio (OR) (95% CI)		1.5750 (0.8181, 3.0320)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1740
Risk Difference (RD) (95% CI)		0.0291 (-0.0126, 0.0709)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1711

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.6
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events - Total and by Severity
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with severe events (Maximum Grade 3/4/5)	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901
Subjects with serious events	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.7
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events - Total and by Severity
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with any Treatment-emergent Rash Events	23 (7.96)	36 (12.68)
Relative Risk (RR) (95% CI)		1.5928 (0.9691, 2.6179)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0664
Odds Ratio (OR) (95% CI)		1.6788 (0.9676, 2.9129)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0654
Risk Difference (RD) (95% CI)		0.0472 (-0.0025, 0.0969)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0629
Subjects with non-severe events (Maximum Grade 1/2)	23 (7.96)	35 (12.32)
Relative Risk (RR) (95% CI)		1.5485 (0.9393, 2.5530)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0865
Odds Ratio (OR) (95% CI)		1.6256 (0.9344, 2.8282)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0855
Risk Difference (RD) (95% CI)		0.0437 (-0.0057, 0.0930)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0829

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.7
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events - Total and by Severity
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with severe events (Maximum Grade 3/4/5)	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.8
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events - Total and by Severity
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with any Treatment-emergent Cataract Events	4 (1.38)	3 (1.06)
Relative Risk (RR) (95% CI)		0.7632 (0.1724, 3.3795)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7219
Odds Ratio (OR) (95% CI)		0.7607 (0.1687, 3.4296)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7218
Risk Difference (RD) (95% CI)		-0.0033 (-0.0212, 0.0147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7207
Subjects with non-severe events (Maximum Grade 1/2)	4 (1.38)	3 (1.06)
Relative Risk (RR) (95% CI)		0.7632 (0.1724, 3.3795)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7219
Odds Ratio (OR) (95% CI)		0.7607 (0.1687, 3.4296)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7218
Risk Difference (RD) (95% CI)		-0.0033 (-0.0212, 0.0147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7207

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.8
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events - Total and by Severity
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.9
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events - Total and by Severity
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	11 (3.81)	3 (1.06)
Relative Risk (RR) (95% CI)		0.2775 (0.0782, 0.9843)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0472
Odds Ratio (OR) (95% CI)		0.2698 (0.0745, 0.9776)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0461
Risk Difference (RD) (95% CI)		-0.0275 (-0.0526, -0.0024)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0315
Subjects with non-severe events (Maximum Grade 1/2)	11 (3.81)	3 (1.06)
Relative Risk (RR) (95% CI)		0.2775 (0.0782, 0.9843)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0472
Odds Ratio (OR) (95% CI)		0.2698 (0.0745, 0.9776)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0461
Risk Difference (RD) (95% CI)		-0.0275 (-0.0526, -0.0024)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0315

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.9
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events - Total and by Severity
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.10
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events - Total and by Severity
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	31 (10.73)	38 (13.38)
Relative Risk (RR) (95% CI)		1.2474 (0.7992, 1.9469)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3305
Odds Ratio (OR) (95% CI)		1.2856 (0.7755, 2.1313)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3300
Risk Difference (RD) (95% CI)		0.0265 (-0.0268, 0.0798)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3291
Subjects with non-severe events (Maximum Grade 1/2)	28 (9.69)	36 (12.68)
Relative Risk (RR) (95% CI)		1.3084 (0.8211, 2.0848)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2582
Odds Ratio (OR) (95% CI)		1.3531 (0.8016, 2.2841)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2576
Risk Difference (RD) (95% CI)		0.0299 (-0.0217, 0.0815)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2563

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.10
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events - Total and by Severity
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with severe events (Maximum Grade 3/4/5)	3 (1.04)	2 (0.70)
Relative Risk (RR) (95% CI)		0.6784 (0.1142, 4.0296)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6695
Odds Ratio (OR) (95% CI)		0.6761 (0.1121, 4.0770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6694
Risk Difference (RD) (95% CI)		-0.0033 (-0.0185, 0.0119)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6669
Subjects with serious events	2 (0.69)	1 (0.35)
Relative Risk (RR) (95% CI)		0.5088 (0.0464, 5.5799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5803
Odds Ratio (OR) (95% CI)		0.5071 (0.0457, 5.6235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5801
Risk Difference (RD) (95% CI)		-0.0034 (-0.0152, 0.0084)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5717

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.11
Study VX20-121-103: Summary of Death
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)

No data met the criteria for this table.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.12
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events - Total and by Severity
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	88 (30.45)	76 (26.76)
Relative Risk (RR) (95% CI)		0.8788 (0.6779, 1.1393)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3295
Odds Ratio (OR) (95% CI)		0.8346 (0.5805, 1.1998)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3289
Risk Difference (RD) (95% CI)		-0.0369 (-0.1108, 0.0370)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3281
Subjects with non-severe events (Maximum Grade 1/2)	80 (27.68)	63 (22.18)
Relative Risk (RR) (95% CI)		0.8014 (0.6016, 1.0674)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1300
Odds Ratio (OR) (95% CI)		0.7447 (0.5091, 1.0895)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1290
Risk Difference (RD) (95% CI)		-0.0550 (-0.1257, 0.0157)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1273

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.12
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events - Total and by Severity
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with severe events (Maximum Grade 3/4/5)	8 (2.77)	13 (4.58)
Relative Risk (RR) (95% CI)		1.6536 (0.6960, 3.9288)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2546
Odds Ratio (OR) (95% CI)		1.6850 (0.6875, 4.1294)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2540
Risk Difference (RD) (95% CI)		0.0181 (-0.0127, 0.0489)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2496
Subjects with serious events	12 (4.15)	18 (6.34)
Relative Risk (RR) (95% CI)		1.5264 (0.7491, 3.1104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2442
Odds Ratio (OR) (95% CI)		1.5620 (0.7382, 3.3054)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2435
Risk Difference (RD) (95% CI)		0.0219 (-0.0146, 0.0584)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2405

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Subjects with any TEAEs	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.2497
Age at screening (<18 years vs. ≥18 years)	0.9229
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.4758
Sex (Male vs. Female)	0.2889
Region (North America vs. Rest of the World)	0.1362

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Infections and infestations	
Influenza	
ppFEV1 at baseline (<70 % vs. ≥70 %)	0.1042
Age at screening (<18 years vs. ≥18 years)	0.3127
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.0666
Sex (Male vs. Female)	0.9306
Region (North America vs. Rest of the World)	0.6355
Sinusitis	
ppFEV1 at baseline (<70 % vs. ≥70 %)	0.8788
Age at screening (<18 years vs. ≥18 years)	0.4140
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.0240
Sex (Male vs. Female)	0.9805

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Region (North America vs. Rest of the World)	0.0923

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Skin and subcutaneous tissue disorders	
Rash	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.0419
Age at screening (<18 years vs. ≥18 years)	0.7391
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.0084
Sex (Male vs. Female)	0.9622
Region (North America vs. Rest of the World)	0.5578

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Psychiatric disorders	
Anxiety	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.8901
Age at screening (<18 years vs. ≥18 years)	0.0874
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.1645
Sex (Male vs. Female)	0.1645
Region (North America vs. Rest of the World)	0.1909

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with any TEAEs	160 (95.81)	149 (96.75)
Relative Risk (RR) (95% CI)		1.0099 (0.9674, 1.0542)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6542
Odds Ratio (OR) (95% CI)		1.3038 (0.4050, 4.1970)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6566
Risk Difference (RD) (95% CI)		0.0094 (-0.0319, 0.0508)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6540
Infections and infestations		
Influenza	5 (2.99)	17 (11.04)
Relative Risk (RR) (95% CI)		3.6870 (1.3938, 9.7533)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0086

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- A subject with multiple events within a category is counted only once in that category.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Odds Ratio (OR) (95% CI)		4.0204 (1.4458, 11.1801)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0077
Risk Difference (RD) (95% CI)		0.0804 (0.0246, 0.1363)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0047
Sinusitis	16 (9.58)	5 (3.25)
Relative Risk (RR) (95% CI)		0.3389 (0.1272, 0.9029)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0305
Odds Ratio (OR) (95% CI)		0.3167 (0.1131, 0.8865)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0286
Risk Difference (RD) (95% CI)		-0.0633 (-0.1160, -0.0107)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0185

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Skin and subcutaneous tissue disorders		
Rash	11 (6.59)	12 (7.79)
Relative Risk (RR) (95% CI)		1.1830 (0.5378, 2.6022)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6761
Odds Ratio (OR) (95% CI)		1.1985 (0.5127, 2.8015)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6760
Risk Difference (RD) (95% CI)		0.0121 (-0.0446, 0.0687)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6766
Psychiatric disorders		
Anxiety	3 (1.80)	8 (5.19)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Relative Risk (RR) (95% CI)		2.8918 (0.7813, 10.7036)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1118
Odds Ratio (OR) (95% CI)		2.9954 (0.7800, 11.5029)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1100
Risk Difference (RD) (95% CI)		0.0340 (-0.0064, 0.0744)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0994

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with any TEAEs	108 (90.76)	120 (96.00)
Relative Risk (RR) (95% CI)		1.0578 (0.9886, 1.1317)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1034
Odds Ratio (OR) (95% CI)		2.4444 (0.8230, 7.2604)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1076
Risk Difference (RD) (95% CI)		0.0524 (-0.0099, 0.1148)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0993
Infections and infestations		
Influenza	11 (9.24)	16 (12.80)
Relative Risk (RR) (95% CI)		1.3847 (0.6703, 2.8604)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3792

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Odds Ratio (OR) (95% CI)		1.4412 (0.6395, 3.2477)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3780
Risk Difference (RD) (95% CI)		0.0356 (-0.0428, 0.1139)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3736
Sinusitis	10 (8.40)	4 (3.20)
Relative Risk (RR) (95% CI)		0.3808 (0.1228, 1.1812)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0946
Odds Ratio (OR) (95% CI)		0.3603 (0.1098, 1.1821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0922
Risk Difference (RD) (95% CI)		-0.0520 (-0.1107, 0.0066)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0819

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline ≥70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Skin and subcutaneous tissue disorders		
Rash	2 (1.68)	12 (9.60)
Relative Risk (RR) (95% CI)		5.7120 (1.3058, 24.9861)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0206
Odds Ratio (OR) (95% CI)		6.2124 (1.3599, 28.3790)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0184
Risk Difference (RD) (95% CI)		0.0792 (0.0226, 0.1358)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0061
Psychiatric disorders		
Anxiety	3 (2.52)	8 (6.40)

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Relative Risk (RR) (95% CI)		2.5387 (0.6898, 9.3426)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1611
Odds Ratio (OR) (95% CI)		2.6439 (0.6844, 10.2141)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1586
Risk Difference (RD) (95% CI)		0.0388 (-0.0125, 0.0901)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1385

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with any TEAEs	34 (89.47)	38 (92.68)
Relative Risk (RR) (95% CI)		1.0359 (0.9015, 1.1902)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6190
Odds Ratio (OR) (95% CI)		1.4902 (0.3110, 7.1401)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6178
Risk Difference (RD) (95% CI)		0.0321 (-0.0939, 0.1581)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6176
Infections and infestations		
Influenza	4 (10.53)	5 (12.20)
Relative Risk (RR) (95% CI)		1.1585 (0.3358, 3.9974)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8159

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Odds Ratio (OR) (95% CI)		1.1806 (0.2923, 4.7675)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8157
Risk Difference (RD) (95% CI)		0.0167 (-0.1231, 0.1565)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8151
Sinusitis	1 (2.63)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0263 (-0.0772, 0.0246)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3109

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Skin and subcutaneous tissue disorders		
Rash	1 (2.63)	3 (7.32)
Relative Risk (RR) (95% CI)		2.7805 (0.3021, 25.5937)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3665
Odds Ratio (OR) (95% CI)		2.9211 (0.2905, 29.3691)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3627
Risk Difference (RD) (95% CI)		0.0469 (-0.0477, 0.1414)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3315
Psychiatric disorders		
Anxiety	1 (2.63)	0

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0263 (-0.0772, 0.0246)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3109

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with any TEAEs	237 (94.42)	236 (97.12)
Relative Risk (RR) (95% CI)		1.0286 (0.9911, 1.0674)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1363
Odds Ratio (OR) (95% CI)		1.9916 (0.7897, 5.0225)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1444
Risk Difference (RD) (95% CI)		0.0270 (-0.0084, 0.0623)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1346
Infections and infestations		
Influenza	12 (4.78)	28 (11.52)
Relative Risk (RR) (95% CI)		2.4102 (1.2546, 4.6299)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0083

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Odds Ratio (OR) (95% CI)		2.5938 (1.2869, 5.2280)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0077
Risk Difference (RD) (95% CI)		0.0674 (0.0194, 0.1155)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0060
Sinusitis	25 (9.96)	9 (3.70)
Relative Risk (RR) (95% CI)		0.3719 (0.1772, 0.7803)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0089
Odds Ratio (OR) (95% CI)		0.3477 (0.1588, 0.7612)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0082
Risk Difference (RD) (95% CI)		-0.0626 (-0.1066, -0.0186)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0053

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Skin and subcutaneous tissue disorders		
Rash	12 (4.78)	22 (9.05)
Relative Risk (RR) (95% CI)		1.8937 (0.9585, 3.7413)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0661
Odds Ratio (OR) (95% CI)		1.9827 (0.9586, 4.1009)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0649
Risk Difference (RD) (95% CI)		0.0427 (-0.0020, 0.0874)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0610
Psychiatric disorders		
Anxiety	5 (1.99)	16 (6.58)

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Relative Risk (RR) (95% CI)		3.3053 (1.2299, 8.8828)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0178
Odds Ratio (OR) (95% CI)		3.4678 (1.2502, 9.6195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0169
Risk Difference (RD) (95% CI)		0.0459 (0.0103, 0.0816)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0116

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with any TEAEs	75 (93.75)	71 (98.61)
Relative Risk (RR) (95% CI)		1.0519 (0.9878, 1.1201)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1150
Odds Ratio (OR) (95% CI)		4.7333 (0.5397, 41.5149)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1605
Risk Difference (RD) (95% CI)		0.0486 (-0.0109, 0.1081)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1095
Infections and infestations		
Influenza	2 (2.50)	11 (15.28)
Relative Risk (RR) (95% CI)		6.1111 (1.4014, 26.6481)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0160

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Odds Ratio (OR) (95% CI)		7.0328 (1.5025, 32.9178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0132
Risk Difference (RD) (95% CI)		0.1278 (0.0379, 0.2176)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0053
Sinusitis	8 (10.00)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.1000 (-0.1657, -0.0343)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0029

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Psychiatric disorders		
Anxiety	1 (1.25)	7 (9.72)
Relative Risk (RR) (95% CI)		7.7778 (0.9805, 61.6966)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0522
Odds Ratio (OR) (95% CI)		8.5077 (1.0203, 70.9383)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0479
Risk Difference (RD) (95% CI)		0.0847 (0.0121, 0.1574)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0222
Skin and subcutaneous tissue disorders		
Rash	7 (8.75)	3 (4.17)

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Relative Risk (RR) (95% CI)		0.4762 (0.1279, 1.7728)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2686
Odds Ratio (OR) (95% CI)		0.4534 (0.1127, 1.8240)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2654
Risk Difference (RD) (95% CI)		-0.0458 (-0.1231, 0.0314)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2448

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with any TEAEs	189 (93.56)	201 (95.71)
Relative Risk (RR) (95% CI)		1.0230 (0.9769, 1.0713)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3343
Odds Ratio (OR) (95% CI)		1.5362 (0.6418, 3.6769)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3350
Risk Difference (RD) (95% CI)		0.0215 (-0.0220, 0.0650)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3331
Infections and infestations		
Influenza	13 (6.44)	21 (10.00)
Relative Risk (RR) (95% CI)		1.5538 (0.7998, 3.0189)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1934

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Odds Ratio (OR) (95% CI)		1.6154 (0.7859, 3.3203)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1920
Risk Difference (RD) (95% CI)		0.0356 (-0.0172, 0.0885)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1861
Sinusitis	18 (8.91)	9 (4.29)
Relative Risk (RR) (95% CI)		0.4810 (0.2212, 1.0455)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0647
Odds Ratio (OR) (95% CI)		0.4577 (0.2006, 1.0442)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0633
Risk Difference (RD) (95% CI)		-0.0463 (-0.0941, 0.0016)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0584

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Skin and subcutaneous tissue disorders		
Rash	6 (2.97)	22 (10.48)
Relative Risk (RR) (95% CI)		3.5270 (1.4603, 8.5184)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0051
Odds Ratio (OR) (95% CI)		3.8227 (1.5164, 9.6365)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0045
Risk Difference (RD) (95% CI)		0.0751 (0.0275, 0.1226)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0020
Psychiatric disorders		
Anxiety	5 (2.48)	9 (4.29)

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Relative Risk (RR) (95% CI)		1.7314 (0.5903, 5.0782)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3174
Odds Ratio (OR) (95% CI)		1.7642 (0.5810, 5.3571)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3165
Risk Difference (RD) (95% CI)		0.0181 (-0.0167, 0.0529)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3076

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Male

System Organ Class Preferred Term	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with any TEAEs	138 (95.83)	144 (96.64)
Relative Risk (RR) (95% CI)		1.0085 (0.9638, 1.0552)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7156
Odds Ratio (OR) (95% CI)		1.2522 (0.3736, 4.1973)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7156
Risk Difference (RD) (95% CI)		0.0081 (-0.0355, 0.0517)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7155
Infections and infestations		
Influenza	9 (6.25)	19 (12.75)
Relative Risk (RR) (95% CI)		2.0403 (0.9548, 4.3597)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0657

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Male

System Organ Class Preferred Term	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Odds Ratio (OR) (95% CI)		2.1923 (0.9570, 5.0220)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0634
Risk Difference (RD) (95% CI)		0.0650 (-0.0016, 0.1316)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0556
Sinusitis	11 (7.64)	4 (2.68)
Relative Risk (RR) (95% CI)		0.3514 (0.1145, 1.0784)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0675
Odds Ratio (OR) (95% CI)		0.3335 (0.1037, 1.0729)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0655
Risk Difference (RD) (95% CI)		-0.0495 (-0.1001, 0.0010)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0548

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Male

System Organ Class Preferred Term	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Skin and subcutaneous tissue disorders		
Rash	6 (4.17)	12 (8.05)
Relative Risk (RR) (95% CI)		1.9329 (0.7454, 5.0121)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1752
Odds Ratio (OR) (95% CI)		2.0146 (0.7352, 5.5207)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1733
Risk Difference (RD) (95% CI)		0.0389 (-0.0157, 0.0934)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1624
Psychiatric disorders		
Anxiety	0	3 (2.01)

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Male

System Organ Class Preferred Term	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0201 (-0.0024, 0.0427)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0802

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Female

System Organ Class Preferred Term	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with any TEAEs	133 (91.72)	130 (96.30)
Relative Risk (RR) (95% CI)		1.0498 (0.9897, 1.1137)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1063
Odds Ratio (OR) (95% CI)		2.3459 (0.8039, 6.8453)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1186
Risk Difference (RD) (95% CI)		0.0457 (-0.0093, 0.1007)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1033
Infections and infestations		
Influenza	7 (4.83)	14 (10.37)
Relative Risk (RR) (95% CI)		2.1481 (0.8942, 5.1608)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0873

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Female

System Organ Class Preferred Term	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Odds Ratio (OR) (95% CI)		2.2810 (0.8914, 5.8367)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0854
Risk Difference (RD) (95% CI)		0.0554 (-0.0067, 0.1176)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0804
Sinusitis	15 (10.34)	5 (3.70)
Relative Risk (RR) (95% CI)		0.3580 (0.1338, 0.9583)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0409
Odds Ratio (OR) (95% CI)		0.3333 (0.1177, 0.9439)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0386
Risk Difference (RD) (95% CI)		-0.0664 (-0.1253, -0.0075)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0272

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Female

System Organ Class Preferred Term	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Skin and subcutaneous tissue disorders		
Rash	7 (4.83)	13 (9.63)
Relative Risk (RR) (95% CI)		1.9947 (0.8204, 4.8498)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1277
Odds Ratio (OR) (95% CI)		2.1007 (0.8120, 5.4350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1259
Risk Difference (RD) (95% CI)		0.0480 (-0.0128, 0.1088)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1215
Psychiatric disorders		
Anxiety	6 (4.14)	13 (9.63)

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Female

System Organ Class Preferred Term	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Relative Risk (RR) (95% CI)		2.3272 (0.9104, 5.9486)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0777
Odds Ratio (OR) (95% CI)		2.4686 (0.9105, 6.6931)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0758
Risk Difference (RD) (95% CI)		0.0549 (-0.0045, 0.1143)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0699

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = North America

System Organ Class Preferred Term	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with any TEAEs	100 (97.09)	110 (96.49)
Relative Risk (RR) (95% CI)		0.9939 (0.9469, 1.0432)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8031
Odds Ratio (OR) (95% CI)		0.8250 (0.1802, 3.7768)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8042
Risk Difference (RD) (95% CI)		-0.0060 (-0.0528, 0.0409)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8031
Infections and infestations		
Influenza	5 (4.85)	14 (12.28)
Relative Risk (RR) (95% CI)		2.5298 (0.9440, 6.7794)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0650

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = North America

System Organ Class Preferred Term	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Odds Ratio (OR) (95% CI)		2.7440 (0.9522, 7.9079)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0616
Risk Difference (RD) (95% CI)		0.0743 (0.0011, 0.1474)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0466
Sinusitis	8 (7.77)	6 (5.26)
Relative Risk (RR) (95% CI)		0.6776 (0.2433, 1.8875)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4565
Odds Ratio (OR) (95% CI)		0.6597 (0.2210, 1.9697)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4561
Risk Difference (RD) (95% CI)		-0.0250 (-0.0910, 0.0409)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4569

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = North America

System Organ Class Preferred Term	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Skin and subcutaneous tissue disorders		
Rash	3 (2.91)	9 (7.89)
Relative Risk (RR) (95% CI)		2.7105 (0.7542, 9.7409)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1266
Odds Ratio (OR) (95% CI)		2.8571 (0.7519, 10.8575)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1233
Risk Difference (RD) (95% CI)		0.0498 (-0.0094, 0.1090)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0991
Psychiatric disorders		
Anxiety	3 (2.91)	4 (3.51)

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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = North America

System Organ Class Preferred Term	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Relative Risk (RR) (95% CI)		1.2047 (0.2761, 5.2554)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8043
Odds Ratio (OR) (95% CI)		1.2121 (0.2648, 5.5490)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8042
Risk Difference (RD) (95% CI)		0.0060 (-0.0409, 0.0528)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8031

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

System Organ Class Preferred Term	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any TEAEs	171 (91.94)	164 (96.47)
Relative Risk (RR) (95% CI)		1.0493 (0.9968, 1.1046)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0662
Odds Ratio (OR) (95% CI)		2.3977 (0.9083, 6.3292)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0774
Risk Difference (RD) (95% CI)		0.0454 (-0.0026, 0.0933)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0639
Infections and infestations		
Influenza	11 (5.91)	19 (11.18)
Relative Risk (RR) (95% CI)		1.8898 (0.9265, 3.8549)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0801

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

System Organ Class Preferred Term	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Odds Ratio (OR) (95% CI)		2.0018 (0.9233, 4.3400)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0788
Risk Difference (RD) (95% CI)		0.0526 (-0.0056, 0.1109)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0766
Sinusitis	18 (9.68)	3 (1.76)
Relative Risk (RR) (95% CI)		0.1824 (0.0547, 0.6081)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0056
Odds Ratio (OR) (95% CI)		0.1677 (0.0485, 0.5799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0048
Risk Difference (RD) (95% CI)		-0.0791 (-0.1260, -0.0323)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0009

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

System Organ Class Preferred Term	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Skin and subcutaneous tissue disorders		
Rash	10 (5.38)	16 (9.41)
Relative Risk (RR) (95% CI)		1.7506 (0.8169, 3.7516)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1499
Odds Ratio (OR) (95% CI)		1.8286 (0.8060, 4.1482)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1487
Risk Difference (RD) (95% CI)		0.0404 (-0.0142, 0.0949)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1472
Psychiatric disorders		
Anxiety	3 (1.61)	12 (7.06)

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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

System Organ Class Preferred Term	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Relative Risk (RR) (95% CI)		4.3765 (1.2565, 15.2440)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0204
Odds Ratio (OR) (95% CI)		4.6329 (1.2844, 16.7118)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0192
Risk Difference (RD) (95% CI)		0.0545 (0.0119, 0.0970)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0121

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Table 2.3.2.2.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Grade 3/4/5 TEAEs by SOC and PT
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Subjects with any Grade 3/4/5 TEAEs	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.0671
Age at screening (<18 years vs. ≥18 years)	0.5119
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.8152
Sex (Male vs. Female)	0.2189
Region (North America vs. Rest of the World)	0.6222

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by "*".
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with any Grade 3/4/5 TEAEs	21 (12.57)	11 (7.14)
Relative Risk (RR) (95% CI)		0.5680 (0.2832, 1.1391)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1111
Odds Ratio (OR) (95% CI)		0.5348 (0.2488, 1.1494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1089
Risk Difference (RD) (95% CI)		-0.0543 (-0.1190, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0998

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Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with any Grade 3/4/5 TEAEs	8 (6.72)	13 (10.40)
Relative Risk (RR) (95% CI)		1.5470 (0.6651, 3.5985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3111
Odds Ratio (OR) (95% CI)		1.6105 (0.6424, 4.0372)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3095
Risk Difference (RD) (95% CI)		0.0368 (-0.0331, 0.1067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3026

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Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with any Grade 3/4/5 TEAEs	5 (13.16)	3 (7.32)
Relative Risk (RR) (95% CI)		0.5561 (0.1425, 2.1702)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3983
Odds Ratio (OR) (95% CI)		0.5211 (0.1156, 2.3479)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3960
Risk Difference (RD) (95% CI)		-0.0584 (-0.1922, 0.0754)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3923

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with any Grade 3/4/5 TEAEs	24 (9.56)	21 (8.64)
Relative Risk (RR) (95% CI)		0.9038 (0.5171, 1.5798)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7226
Odds Ratio (OR) (95% CI)		0.8947 (0.4841, 1.6535)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7226
Risk Difference (RD) (95% CI)		-0.0092 (-0.0599, 0.0415)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7222

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with any Grade 3/4/5 TEAEs	6 (7.50)	5 (6.94)
Relative Risk (RR) (95% CI)		0.9259 (0.2951, 2.9048)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8950
Odds Ratio (OR) (95% CI)		0.9204 (0.2685, 3.1551)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8950
Risk Difference (RD) (95% CI)		-0.0056 (-0.0879, 0.0768)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8948

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with any Grade 3/4/5 TEAEs	23 (11.39)	19 (9.05)
Relative Risk (RR) (95% CI)		0.7946 (0.4466, 1.4137)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4341
Odds Ratio (OR) (95% CI)		0.7742 (0.4078, 1.4696)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4338
Risk Difference (RD) (95% CI)		-0.0234 (-0.0819, 0.0351)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4335

- MedDRA version 26.1.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Male

System Organ Class Preferred Term	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with any Grade 3/4/5 TEAEs	16 (11.11)	10 (6.71)
Relative Risk (RR) (95% CI)		0.6040 (0.2836, 1.2866)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1913
Odds Ratio (OR) (95% CI)		0.5755 (0.2520, 1.3143)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1898
Risk Difference (RD) (95% CI)		-0.0440 (-0.1092, 0.0212)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1859

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Female

System Organ Class Preferred Term	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with any Grade 3/4/5 TEAEs	13 (8.97)	14 (10.37)
Relative Risk (RR) (95% CI)		1.1567 (0.5644, 2.3706)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6909
Odds Ratio (OR) (95% CI)		1.1748 (0.5310, 2.5995)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6909
Risk Difference (RD) (95% CI)		0.0140 (-0.0553, 0.0834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6913

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = North America

System Organ Class Preferred Term	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with any Grade 3/4/5 TEAEs	9 (8.74)	10 (8.77)
Relative Risk (RR) (95% CI)		1.0039 (0.4247, 2.3729)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9929
Odds Ratio (OR) (95% CI)		1.0043 (0.3912, 2.5780)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9929
Risk Difference (RD) (95% CI)		0.0003 (-0.0750, 0.0756)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9929

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

System Organ Class Preferred Term	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any Grade 3/4/5 TEAEs	20 (10.75)	14 (8.24)
Relative Risk (RR) (95% CI)		0.7659 (0.3996, 1.4679)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4216
Odds Ratio (OR) (95% CI)		0.7449 (0.3636, 1.5259)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4208
Risk Difference (RD) (95% CI)		-0.0252 (-0.0859, 0.0356)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4166

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Serious TEAEs by SOC and PT
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Subjects with any TEAEs	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.7126
Age at screening (<18 years vs. ≥18 years)	0.0336
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.4743
Sex (Male vs. Female)	0.3740
Region (North America vs. Rest of the World)	0.2542

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by "*".
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with any serious TEAEs	21 (12.57)	15 (9.74)
Relative Risk (RR) (95% CI)		0.7746 (0.4145, 1.4476)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4234
Odds Ratio (OR) (95% CI)		0.7503 (0.3718, 1.5140)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4225
Risk Difference (RD) (95% CI)		-0.0283 (-0.0971, 0.0404)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4188

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline ≥70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with any serious TEAEs	12 (10.08)	8 (6.40)
Relative Risk (RR) (95% CI)		0.6347 (0.2689, 1.4978)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2994
Odds Ratio (OR) (95% CI)		0.6097 (0.2400, 1.5487)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2982
Risk Difference (RD) (95% CI)		-0.0368 (-0.1059, 0.0322)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2957

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- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with any serious TEAEs	7 (18.42)	1 (2.44)
Relative Risk (RR) (95% CI)		0.1324 (0.0171, 1.0267)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0530
Odds Ratio (OR) (95% CI)		0.1107 (0.0129, 0.9477)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0445
Risk Difference (RD) (95% CI)		-0.1598 (-0.2918, -0.0278)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0176

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with any serious TEAEs	26 (10.36)	22 (9.05)
Relative Risk (RR) (95% CI)		0.8740 (0.5095, 1.4993)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6248
Odds Ratio (OR) (95% CI)		0.8615 (0.4740, 1.5655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6246
Risk Difference (RD) (95% CI)		-0.0131 (-0.0652, 0.0391)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6240

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with any serious TEAEs	8 (10.00)	7 (9.72)
Relative Risk (RR) (95% CI)		0.9722 (0.3711, 2.5471)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9543
Odds Ratio (OR) (95% CI)		0.9692 (0.3330, 2.8211)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9543
Risk Difference (RD) (95% CI)		-0.0028 (-0.0977, 0.0921)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9542

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with any serious TEAEs	24 (11.88)	16 (7.62)
Relative Risk (RR) (95% CI)		0.6413 (0.3511, 1.1712)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1483
Odds Ratio (OR) (95% CI)		0.6117 (0.3147, 1.1888)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1471
Risk Difference (RD) (95% CI)		-0.0426 (-0.0999, 0.0146)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1446

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Male

System Organ Class Preferred Term	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with any serious TEAEs	14 (9.72)	13 (8.72)
Relative Risk (RR) (95% CI)		0.8974 (0.4371, 1.8424)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7680
Odds Ratio (OR) (95% CI)		0.8876 (0.4019, 1.9602)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7680
Risk Difference (RD) (95% CI)		-0.0100 (-0.0763, 0.0563)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7681

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Female

System Organ Class Preferred Term	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with any serious TEAEs	19 (13.10)	10 (7.41)
Relative Risk (RR) (95% CI)		0.5653 (0.2727, 1.1718)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1251
Odds Ratio (OR) (95% CI)		0.5305 (0.2373, 1.1863)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1226
Risk Difference (RD) (95% CI)		-0.0570 (-0.1274, 0.0135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1132

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = North America

System Organ Class Preferred Term	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with any serious TEAEs	6 (5.83)	8 (7.02)
Relative Risk (RR) (95% CI)		1.2047 (0.4325, 3.3556)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7216
Odds Ratio (OR) (95% CI)		1.2201 (0.4087, 3.6426)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7214
Risk Difference (RD) (95% CI)		0.0119 (-0.0532, 0.0771)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7198

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

System Organ Class Preferred Term	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any serious TEAEs	27 (14.52)	15 (8.82)
Relative Risk (RR) (95% CI)		0.6078 (0.3350, 1.1031)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1016
Odds Ratio (OR) (95% CI)		0.5699 (0.2920, 1.1124)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0994
Risk Difference (RD) (95% CI)		-0.0569 (-0.1231, 0.0093)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0918

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for TEAEs Leading to Treatment Discontinuation
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any TEAEs leading to treatment discontinuation	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.0573
Age at screening (<18 years vs. ≥18 years)	0.2529
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.1237
Sex (Male vs. Female)	0.2039
Region (North America vs. Rest of the World)	0.5161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with any TEAEs leading to treatment discontinuation	8 (4.79)	7 (4.55)
Relative Risk (RR) (95% CI)		0.9489 (0.3524, 2.5548)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9173
Odds Ratio (OR) (95% CI)		0.9464 (0.3349, 2.6746)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9173
Risk Difference (RD) (95% CI)		-0.0024 (-0.0486, 0.0437)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9172

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with any TEAEs leading to treatment discontinuation	1 (0.84)	7 (5.60)
Relative Risk (RR) (95% CI)		6.6640 (0.8324, 53.3524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0739
Odds Ratio (OR) (95% CI)		7.0000 (0.8480, 57.7821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0708
Risk Difference (RD) (95% CI)		0.0476 (0.0041, 0.0911)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0321

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with any TEAEs leading to treatment discontinuation	2 (5.26)	1 (2.44)
Relative Risk (RR) (95% CI)		0.4634 (0.0438, 4.9057)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5229
Odds Ratio (OR) (95% CI)		0.4500 (0.0391, 5.1749)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5217
Risk Difference (RD) (95% CI)		-0.0282 (-0.1135, 0.0570)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5162

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with any TEAEs leading to treatment discontinuation	7 (2.79)	13 (5.35)
Relative Risk (RR) (95% CI)		1.9183 (0.7785, 4.7265)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1568
Odds Ratio (OR) (95% CI)		1.9702 (0.7724, 5.0252)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1558
Risk Difference (RD) (95% CI)		0.0256 (-0.0093, 0.0605)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1499

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with any TEAEs leading to treatment discontinuation	1 (1.25)	5 (6.94)
Relative Risk (RR) (95% CI)		5.5556 (0.6646, 46.4368)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1134
Odds Ratio (OR) (95% CI)		5.8955 (0.6721, 51.7157)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1093
Risk Difference (RD) (95% CI)		0.0569 (-0.0066, 0.1205)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0791

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with any TEAEs leading to treatment discontinuation	8 (3.96)	9 (4.29)
Relative Risk (RR) (95% CI)		1.0821 (0.4259, 2.7498)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8682
Odds Ratio (OR) (95% CI)		1.0858 (0.4106, 2.8718)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8682
Risk Difference (RD) (95% CI)		0.0033 (-0.0351, 0.0416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8681

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with any TEAEs leading to treatment discontinuation	6 (4.17)	6 (4.03)
Relative Risk (RR) (95% CI)		0.9664 (0.3191, 2.9272)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9519
Odds Ratio (OR) (95% CI)		0.9650 (0.3039, 3.0646)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9519
Risk Difference (RD) (95% CI)		-0.0014 (-0.0468, 0.0440)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9519

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with any TEAEs leading to treatment discontinuation	3 (2.07)	8 (5.93)
Relative Risk (RR) (95% CI)		2.8642 (0.7759, 10.5732)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1143
Odds Ratio (OR) (95% CI)		2.9816 (0.7743, 11.4821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1123
Risk Difference (RD) (95% CI)		0.0386 (-0.0075, 0.0846)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1009

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with any TEAEs leading to treatment discontinuation	4 (3.88)	5 (4.39)
Relative Risk (RR) (95% CI)		1.1294 (0.3117, 4.0926)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8531
Odds Ratio (OR) (95% CI)		1.1353 (0.2965, 4.3473)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8530
Risk Difference (RD) (95% CI)		0.0050 (-0.0479, 0.0580)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8525

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any TEAEs leading to treatment discontinuation	5 (2.69)	9 (5.29)
Relative Risk (RR) (95% CI)		1.9694 (0.6733, 5.7603)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2158
Odds Ratio (OR) (95% CI)		2.0236 (0.6645, 6.1628)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2148
Risk Difference (RD) (95% CI)		0.0261 (-0.0148, 0.0670)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2118

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Elevated Transaminase Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any Treatment-emergent Elevated Transaminase Events	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.4815
Age at screening (<18 years vs. ≥18 years)	0.1358
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.7272
Sex (Male vs. Female)	0.6078
Region (North America vs. Rest of the World)	0.4886

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.5.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Elevated Transaminase Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with non-severe events (Maximum Grade 1/2)	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.3160
Age at screening (<18 years vs. ≥18 years)	0.3434
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.7477
Sex (Male vs. Female)	0.9514
Region (North America vs. Rest of the World)	0.4361

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.5.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Elevated Transaminase Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with severe events (Maximum Grade 3/4/5)	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.5.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Elevated Transaminase Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with serious events	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	10 (5.99)	14 (9.09)
Relative Risk (RR) (95% CI)		1.5182 (0.6950, 3.3165)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2950
Odds Ratio (OR) (95% CI)		1.5700 (0.6758, 3.6472)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2942
Risk Difference (RD) (95% CI)		0.0310 (-0.0269, 0.0890)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2938
Subjects with non-severe events (Maximum Grade 1/2)	10 (5.99)	13 (8.44)
Relative Risk (RR) (95% CI)		1.4097 (0.6367, 3.1211)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3971
Odds Ratio (OR) (95% CI)		1.4475 (0.6155, 3.4043)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3966

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Risk Difference (RD) (95% CI)		0.0245 (-0.0322, 0.0813)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3970
Subjects with severe events (Maximum Grade 3/4/5)	0	1 (0.65)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	1 (0.65)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	12 (10.08)	13 (10.40)
Relative Risk (RR) (95% CI)		1.0313 (0.4904, 2.1689)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9352
Odds Ratio (OR) (95% CI)		1.0350 (0.4521, 2.3691)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9352
Risk Difference (RD) (95% CI)		0.0032 (-0.0729, 0.0793)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9351
Subjects with non-severe events (Maximum Grade 1/2)	12 (10.08)	10 (8.00)
Relative Risk (RR) (95% CI)		0.7933 (0.3562, 1.7670)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5710
Odds Ratio (OR) (95% CI)		0.7754 (0.3218, 1.8684)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5707

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Risk Difference (RD) (95% CI)		-0.0208 (-0.0929, 0.0512)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5707
Subjects with severe events (Maximum Grade 3/4/5)	0	3 (2.40)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	1 (0.80)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

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- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once in that category.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	1 (2.63)	5 (12.20)
Relative Risk (RR) (95% CI)		4.6341 (0.5668, 37.8880)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1526
Odds Ratio (OR) (95% CI)		5.1389 (0.5720, 46.1709)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1440
Risk Difference (RD) (95% CI)		0.0956 (-0.0167, 0.2080)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0952
Subjects with non-severe events (Maximum Grade 1/2)	1 (2.63)	3 (7.32)
Relative Risk (RR) (95% CI)		2.7805 (0.3021, 25.5937)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3665
Odds Ratio (OR) (95% CI)		2.9211 (0.2905, 29.3691)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3627

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Risk Difference (RD) (95% CI)		0.0469 (-0.0477, 0.1414)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3315
Subjects with severe events (Maximum Grade 3/4/5)	0	2 (4.88)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

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- A subject with multiple events within a category is counted only once in that category.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	21 (8.37)	22 (9.05)
Relative Risk (RR) (95% CI)		1.0821 (0.6111, 1.9160)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7866
Odds Ratio (OR) (95% CI)		1.0903 (0.5831, 2.0385)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7866
Risk Difference (RD) (95% CI)		0.0069 (-0.0429, 0.0566)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7867
Subjects with non-severe events (Maximum Grade 1/2)	21 (8.37)	20 (8.23)
Relative Risk (RR) (95% CI)		0.9837 (0.5473, 1.7683)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9563
Odds Ratio (OR) (95% CI)		0.9823 (0.5182, 1.8619)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9563

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Risk Difference (RD) (95% CI)		-0.0014 (-0.0500, 0.0473)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9563
Subjects with severe events (Maximum Grade 3/4/5)	0	2 (0.82)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	2 (0.82)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

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- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	7 (8.75)	7 (9.72)
Relative Risk (RR) (95% CI)		1.1111 (0.4095, 3.0146)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8361
Odds Ratio (OR) (95% CI)		1.1231 (0.3740, 3.3728)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8361
Risk Difference (RD) (95% CI)		0.0097 (-0.0826, 0.1020)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8364
Subjects with non-severe events (Maximum Grade 1/2)	7 (8.75)	6 (8.33)
Relative Risk (RR) (95% CI)		0.9524 (0.3356, 2.7023)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9269
Odds Ratio (OR) (95% CI)		0.9481 (0.3032, 2.9647)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9269

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- A subject with multiple events within a category is counted only once in that category.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Risk Difference (RD) (95% CI)		-0.0042 (-0.0931, 0.0848)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9268
Subjects with severe events (Maximum Grade 3/4/5)	0	1 (1.39)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	1 (1.39)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	14 (6.93)	20 (9.52)
Relative Risk (RR) (95% CI)		1.3741 (0.7137, 2.6457)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3416
Odds Ratio (OR) (95% CI)		1.4135 (0.6935, 2.8812)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3408
Risk Difference (RD) (95% CI)		0.0259 (-0.0270, 0.0789)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3371
Subjects with non-severe events (Maximum Grade 1/2)	14 (6.93)	17 (8.10)
Relative Risk (RR) (95% CI)		1.1680 (0.5915, 2.3066)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6546
Odds Ratio (OR) (95% CI)		1.1828 (0.5670, 2.4676)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6545

- MedDRA version 26.1.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Risk Difference (RD) (95% CI)		0.0116 (-0.0392, 0.0625)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6537
Subjects with severe events (Maximum Grade 3/4/5)	0	3 (1.43)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	1 (0.48)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	14 (9.72)	16 (10.74)
Relative Risk (RR) (95% CI)		1.1045 (0.5597, 2.1796)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7744
Odds Ratio (OR) (95% CI)		1.1171 (0.5240, 2.3813)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7743
Risk Difference (RD) (95% CI)		0.0102 (-0.0592, 0.0795)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7741
Subjects with non-severe events (Maximum Grade 1/2)	14 (9.72)	15 (10.07)
Relative Risk (RR) (95% CI)		1.0355 (0.5186, 2.0673)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9213
Odds Ratio (OR) (95% CI)		1.0394 (0.4826, 2.2388)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9213

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Risk Difference (RD) (95% CI)		0.0034 (-0.0649, 0.0718)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9213
Subjects with severe events (Maximum Grade 3/4/5)	0	1 (0.67)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	1 (0.67)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	8 (5.52)	11 (8.15)
Relative Risk (RR) (95% CI)		1.4769 (0.6126, 3.5607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3852
Odds Ratio (OR) (95% CI)		1.5192 (0.5919, 3.8990)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3846
Risk Difference (RD) (95% CI)		0.0263 (-0.0329, 0.0856)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3841
Subjects with non-severe events (Maximum Grade 1/2)	8 (5.52)	8 (5.93)
Relative Risk (RR) (95% CI)		1.0741 (0.4148, 2.7815)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8830
Odds Ratio (OR) (95% CI)		1.0787 (0.3932, 2.9597)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8830

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Risk Difference (RD) (95% CI)		0.0041 (-0.0504, 0.0586)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8831
Subjects with severe events (Maximum Grade 3/4/5)	0	3 (2.22)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	1 (0.74)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	10 (9.71)	11 (9.65)
Relative Risk (RR) (95% CI)		0.9939 (0.4404, 2.2428)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9882
Odds Ratio (OR) (95% CI)		0.9932 (0.4034, 2.4456)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9882
Risk Difference (RD) (95% CI)		-0.0006 (-0.0794, 0.0782)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9882
Subjects with non-severe events (Maximum Grade 1/2)	10 (9.71)	9 (7.89)
Relative Risk (RR) (95% CI)		0.8132 (0.3440, 1.9220)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6375
Odds Ratio (OR) (95% CI)		0.7971 (0.3105, 2.0464)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6374

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Risk Difference (RD) (95% CI)		-0.0181 (-0.0938, 0.0575)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6383
Subjects with severe events (Maximum Grade 3/4/5)	0	2 (1.75)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	1 (0.88)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	12 (6.45)	16 (9.41)
Relative Risk (RR) (95% CI)		1.4588 (0.7108, 2.9941)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3033
Odds Ratio (OR) (95% CI)		1.5065 (0.6911, 3.2839)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3027
Risk Difference (RD) (95% CI)		0.0296 (-0.0267, 0.0859)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3030
Subjects with non-severe events (Maximum Grade 1/2)	12 (6.45)	14 (8.24)
Relative Risk (RR) (95% CI)		1.2765 (0.6075, 2.6820)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5193
Odds Ratio (OR) (95% CI)		1.3013 (0.5843, 2.8983)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5192

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Risk Difference (RD) (95% CI)		0.0178 (-0.0365, 0.0722)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5201
Subjects with severe events (Maximum Grade 3/4/5)	0	2 (1.18)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	1 (0.59)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.5.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Creatine Kinase Elevation Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.6767
Age at screening (<18 years vs. ≥18 years)	0.7207
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.0090
Sex (Male vs. Female)	0.7223
Region (North America vs. Rest of the World)	0.3836

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.6.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Creatine Kinase Elevation Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with non-severe events (Maximum Grade 1/2)	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.6335
Age at screening (<18 years vs. ≥18 years)	0.7098
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.0079
Sex (Male vs. Female)	0.6834
Region (North America vs. Rest of the World)	0.3990

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.6.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Creatine Kinase Elevation Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with severe events (Maximum Grade 3/4/5)	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.6.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Creatine Kinase Elevation Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with serious events	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	9 (5.39)	14 (9.09)
Relative Risk (RR) (95% CI)		1.6869 (0.7517, 3.7853)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2048
Odds Ratio (OR) (95% CI)		1.7556 (0.7372, 4.1809)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2037
Risk Difference (RD) (95% CI)		0.0370 (-0.0199, 0.0939)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2021
Subjects with non-severe events (Maximum Grade 1/2)	8 (4.79)	13 (8.44)
Relative Risk (RR) (95% CI)		1.7622 (0.7509, 4.1356)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1930
Odds Ratio (OR) (95% CI)		1.8324 (0.7380, 4.5498)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1918

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Risk Difference (RD) (95% CI)		0.0365 (-0.0181, 0.0911)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1897
Subjects with severe events (Maximum Grade 3/4/5)	1 (0.60)	1 (0.65)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	1 (0.65)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	8 (6.72)	11 (8.80)
Relative Risk (RR) (95% CI)		1.3090 (0.5454, 3.1415)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5466
Odds Ratio (OR) (95% CI)		1.3388 (0.5191, 3.4531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5461
Risk Difference (RD) (95% CI)		0.0208 (-0.0462, 0.0878)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5435
Subjects with non-severe events (Maximum Grade 1/2)	8 (6.72)	11 (8.80)
Relative Risk (RR) (95% CI)		1.3090 (0.5454, 3.1415)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5466
Odds Ratio (OR) (95% CI)		1.3388 (0.5191, 3.4531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5461

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Risk Difference (RD) (95% CI)		0.0208 (-0.0462, 0.0878)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5435
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	1 (2.63)	1 (2.44)
Relative Risk (RR) (95% CI)		0.9268 (0.0601, 14.3029)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9566
Odds Ratio (OR) (95% CI)		0.9250 (0.0558, 15.3278)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9566
Risk Difference (RD) (95% CI)		-0.0019 (-0.0714, 0.0675)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9566
Subjects with non-severe events (Maximum Grade 1/2)	1 (2.63)	1 (2.44)
Relative Risk (RR) (95% CI)		0.9268 (0.0601, 14.3029)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9566
Odds Ratio (OR) (95% CI)		0.9250 (0.0558, 15.3278)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9566

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Risk Difference (RD) (95% CI)		-0.0019 (-0.0714, 0.0675)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9566
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	16 (6.37)	24 (9.88)
Relative Risk (RR) (95% CI)		1.5494 (0.8440, 2.8444)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1577
Odds Ratio (OR) (95% CI)		1.6096 (0.8329, 3.1105)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1568
Risk Difference (RD) (95% CI)		0.0350 (-0.0132, 0.0832)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1542
Subjects with non-severe events (Maximum Grade 1/2)	15 (5.98)	23 (9.47)
Relative Risk (RR) (95% CI)		1.5838 (0.8468, 2.9622)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1500
Odds Ratio (OR) (95% CI)		1.6448 (0.8367, 3.2335)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1490

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Risk Difference (RD) (95% CI)		0.0349 (-0.0122, 0.0819)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1462
Subjects with severe events (Maximum Grade 3/4/5)	1 (0.40)	1 (0.41)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	1 (0.41)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	6 (7.50)	1 (1.39)
Relative Risk (RR) (95% CI)		0.1852 (0.0228, 1.5016)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1143
Odds Ratio (OR) (95% CI)		0.1737 (0.0204, 1.4792)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1092
Risk Difference (RD) (95% CI)		-0.0611 (-0.1248, 0.0026)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0602
Subjects with non-severe events (Maximum Grade 1/2)	6 (7.50)	1 (1.39)
Relative Risk (RR) (95% CI)		0.1852 (0.0228, 1.5016)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1143
Odds Ratio (OR) (95% CI)		0.1737 (0.0204, 1.4792)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1092

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Risk Difference (RD) (95% CI)		-0.0611 (-0.1248, 0.0026)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0602
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	11 (5.45)	24 (11.43)
Relative Risk (RR) (95% CI)		2.0987 (1.0558, 4.1717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0344
Odds Ratio (OR) (95% CI)		2.2405 (1.0672, 4.7036)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0330
Risk Difference (RD) (95% CI)		0.0598 (0.0066, 0.1130)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0275
Subjects with non-severe events (Maximum Grade 1/2)	10 (4.95)	23 (10.95)
Relative Risk (RR) (95% CI)		2.2124 (1.0803, 4.5308)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0299
Odds Ratio (OR) (95% CI)		2.3615 (1.0942, 5.0964)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0286

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Risk Difference (RD) (95% CI)		0.0600 (0.0083, 0.1118)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0230
Subjects with severe events (Maximum Grade 3/4/5)	1 (0.50)	1 (0.48)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	1 (0.48)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	11 (7.64)	18 (12.08)
Relative Risk (RR) (95% CI)		1.5815 (0.7742, 3.2304)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2085
Odds Ratio (OR) (95% CI)		1.6613 (0.7556, 3.6531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2067
Risk Difference (RD) (95% CI)		0.0444 (-0.0236, 0.1124)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2003
Subjects with non-severe events (Maximum Grade 1/2)	10 (6.94)	17 (11.41)
Relative Risk (RR) (95% CI)		1.6430 (0.7786, 3.4669)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1925
Odds Ratio (OR) (95% CI)		1.7258 (0.7622, 3.9075)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1907

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Risk Difference (RD) (95% CI)		0.0446 (-0.0212, 0.1105)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1835
Subjects with severe events (Maximum Grade 3/4/5)	1 (0.69)	1 (0.67)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	1 (0.67)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	6 (4.14)	7 (5.19)
Relative Risk (RR) (95% CI)		1.2531 (0.4320, 3.6347)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6780
Odds Ratio (OR) (95% CI)		1.2669 (0.4148, 3.8696)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6779
Risk Difference (RD) (95% CI)		0.0105 (-0.0390, 0.0600)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6784
Subjects with non-severe events (Maximum Grade 1/2)	6 (4.14)	7 (5.19)
Relative Risk (RR) (95% CI)		1.2531 (0.4320, 3.6347)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6780
Odds Ratio (OR) (95% CI)		1.2669 (0.4148, 3.8696)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6779

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Risk Difference (RD) (95% CI)		0.0105 (-0.0390, 0.0600)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6784
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	4 (3.88)	10 (8.77)
Relative Risk (RR) (95% CI)		2.2588 (0.7308, 6.9819)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1570
Odds Ratio (OR) (95% CI)		2.3798 (0.7227, 7.8363)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1539
Risk Difference (RD) (95% CI)		0.0489 (-0.0151, 0.1128)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1340
Subjects with non-severe events (Maximum Grade 1/2)	4 (3.88)	10 (8.77)
Relative Risk (RR) (95% CI)		2.2588 (0.7308, 6.9819)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1570
Odds Ratio (OR) (95% CI)		2.3798 (0.7227, 7.8363)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1539

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Risk Difference (RD) (95% CI)		0.0489 (-0.0151, 0.1128)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1340
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	13 (6.99)	15 (8.82)
Relative Risk (RR) (95% CI)		1.2624 (0.6188, 2.5755)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5218
Odds Ratio (OR) (95% CI)		1.2878 (0.5941, 2.7917)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5216
Risk Difference (RD) (95% CI)		0.0183 (-0.0379, 0.0746)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5225
Subjects with non-severe events (Maximum Grade 1/2)	12 (6.45)	14 (8.24)
Relative Risk (RR) (95% CI)		1.2765 (0.6075, 2.6820)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5193
Odds Ratio (OR) (95% CI)		1.3013 (0.5843, 2.8983)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5192

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Risk Difference (RD) (95% CI)		0.0178 (-0.0365, 0.0722)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5201
Subjects with severe events (Maximum Grade 3/4/5)	1 (0.54)	1 (0.59)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	1 (0.59)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.6.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Rash Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any Treatment-emergent Rash Events	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.8439
Age at screening (<18 years vs. ≥18 years)	0.9651
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.0159
Sex (Male vs. Female)	0.9289
Region (North America vs. Rest of the World)	0.4968

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.7.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Rash Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with non-severe events (Maximum Grade 1/2)	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.7538
Age at screening (<18 years vs. ≥18 years)	0.9220
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.0187
Sex (Male vs. Female)	0.8460
Region (North America vs. Rest of the World)	0.4523

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.7.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Rash Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with severe events (Maximum Grade 3/4/5)	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.7.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Rash Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with serious events	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with any Treatment-emergent Rash Events	12 (7.19)	18 (11.69)
Relative Risk (RR) (95% CI)		1.6266 (0.8103, 3.2653)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1712
Odds Ratio (OR) (95% CI)		1.7096 (0.7948, 3.6771)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1700
Risk Difference (RD) (95% CI)		0.0450 (-0.0191, 0.1091)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1686
Subjects with non-severe events (Maximum Grade 1/2)	12 (7.19)	18 (11.69)
Relative Risk (RR) (95% CI)		1.6266 (0.8103, 3.2653)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1712
Odds Ratio (OR) (95% CI)		1.7096 (0.7948, 3.6771)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1700

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Risk Difference (RD) (95% CI)		0.0450 (-0.0191, 0.1091)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1686
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with any Treatment-emergent Rash Events	11 (9.24)	17 (13.60)
Relative Risk (RR) (95% CI)		1.4713 (0.7193, 3.0096)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2903
Odds Ratio (OR) (95% CI)		1.5455 (0.6917, 3.4531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2886
Risk Difference (RD) (95% CI)		0.0436 (-0.0359, 0.1231)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2828
Subjects with non-severe events (Maximum Grade 1/2)	11 (9.24)	16 (12.80)
Relative Risk (RR) (95% CI)		1.3847 (0.6703, 2.8604)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3792
Odds Ratio (OR) (95% CI)		1.4412 (0.6395, 3.2477)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3780

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- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Risk Difference (RD) (95% CI)		0.0356 (-0.0428, 0.1139)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3736
Subjects with severe events (Maximum Grade 3/4/5)	0	1 (0.80)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with any Treatment-emergent Rash Events	4 (10.53)	7 (17.07)
Relative Risk (RR) (95% CI)		1.6220 (0.5154, 5.1043)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4083
Odds Ratio (OR) (95% CI)		1.7500 (0.4688, 6.5329)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4050
Risk Difference (RD) (95% CI)		0.0655 (-0.0855, 0.2164)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3953
Subjects with non-severe events (Maximum Grade 1/2)	4 (10.53)	7 (17.07)
Relative Risk (RR) (95% CI)		1.6220 (0.5154, 5.1043)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4083
Odds Ratio (OR) (95% CI)		1.7500 (0.4688, 6.5329)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4050

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Risk Difference (RD) (95% CI)		0.0655 (-0.0855, 0.2164)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3953
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with any Treatment-emergent Rash Events	19 (7.57)	29 (11.93)
Relative Risk (RR) (95% CI)		1.5766 (0.9087, 2.7352)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1053
Odds Ratio (OR) (95% CI)		1.6547 (0.9013, 3.0380)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1042
Risk Difference (RD) (95% CI)		0.0436 (-0.0086, 0.0959)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1017
Subjects with non-severe events (Maximum Grade 1/2)	19 (7.57)	28 (11.52)
Relative Risk (RR) (95% CI)		1.5222 (0.8737, 2.6522)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1380
Odds Ratio (OR) (95% CI)		1.5902 (0.8628, 2.9308)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1370

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- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Risk Difference (RD) (95% CI)		0.0395 (-0.0123, 0.0913)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1347
Subjects with severe events (Maximum Grade 3/4/5)	0	1 (0.41)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with any Treatment-emergent Rash Events	10 (12.50)	5 (6.94)
Relative Risk (RR) (95% CI)		0.5556 (0.1993, 1.5487)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2611
Odds Ratio (OR) (95% CI)		0.5224 (0.1697, 1.6084)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2578
Risk Difference (RD) (95% CI)		-0.0556 (-0.1488, 0.0377)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2430
Subjects with non-severe events (Maximum Grade 1/2)	10 (12.50)	5 (6.94)
Relative Risk (RR) (95% CI)		0.5556 (0.1993, 1.5487)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2611
Odds Ratio (OR) (95% CI)		0.5224 (0.1697, 1.6084)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2578

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Risk Difference (RD) (95% CI)		-0.0556 (-0.1488, 0.0377)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2430
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with any Treatment-emergent Rash Events	13 (6.44)	31 (14.76)
Relative Risk (RR) (95% CI)		2.2938 (1.2362, 4.2561)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0085
Odds Ratio (OR) (95% CI)		2.5178 (1.2767, 4.9655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0077
Risk Difference (RD) (95% CI)		0.0833 (0.0246, 0.1420)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0054
Subjects with non-severe events (Maximum Grade 1/2)	13 (6.44)	30 (14.29)
Relative Risk (RR) (95% CI)		2.2198 (1.1924, 4.1325)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0119
Odds Ratio (OR) (95% CI)		2.4231 (1.2250, 4.7927)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0110

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Risk Difference (RD) (95% CI)		0.0785 (0.0203, 0.1367)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0082
Subjects with severe events (Maximum Grade 3/4/5)	0	1 (0.48)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with any Treatment-emergent Rash Events	10 (6.94)	17 (11.41)
Relative Risk (RR) (95% CI)		1.6430 (0.7786, 3.4669)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1925
Odds Ratio (OR) (95% CI)		1.7258 (0.7622, 3.9075)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1907
Risk Difference (RD) (95% CI)		0.0446 (-0.0212, 0.1105)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1835
Subjects with non-severe events (Maximum Grade 1/2)	10 (6.94)	17 (11.41)
Relative Risk (RR) (95% CI)		1.6430 (0.7786, 3.4669)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1925
Odds Ratio (OR) (95% CI)		1.7258 (0.7622, 3.9075)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1907

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Risk Difference (RD) (95% CI)		0.0446 (-0.0212, 0.1105)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1835
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with any Treatment-emergent Rash Events	13 (8.97)	19 (14.07)
Relative Risk (RR) (95% CI)		1.5698 (0.8070, 3.0536)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1841
Odds Ratio (OR) (95% CI)		1.6631 (0.7870, 3.5147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1827
Risk Difference (RD) (95% CI)		0.0511 (-0.0238, 0.1259)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1810
Subjects with non-severe events (Maximum Grade 1/2)	13 (8.97)	18 (13.33)
Relative Risk (RR) (95% CI)		1.4872 (0.7581, 2.9173)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2483
Odds Ratio (OR) (95% CI)		1.5621 (0.7338, 3.3254)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2472

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Risk Difference (RD) (95% CI)		0.0437 (-0.0301, 0.1175)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2462
Subjects with severe events (Maximum Grade 3/4/5)	0	1 (0.74)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with any Treatment-emergent Rash Events	5 (4.85)	12 (10.53)
Relative Risk (RR) (95% CI)		2.1684 (0.7908, 5.9457)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1326
Odds Ratio (OR) (95% CI)		2.3059 (0.7835, 6.7865)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1293
Risk Difference (RD) (95% CI)		0.0567 (-0.0133, 0.1267)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1121
Subjects with non-severe events (Maximum Grade 1/2)	5 (4.85)	12 (10.53)
Relative Risk (RR) (95% CI)		2.1684 (0.7908, 5.9457)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1326
Odds Ratio (OR) (95% CI)		2.3059 (0.7835, 6.7865)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1293

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Risk Difference (RD) (95% CI)		0.0567 (-0.0133, 0.1267)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1121
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any Treatment-emergent Rash Events	18 (9.68)	24 (14.12)
Relative Risk (RR) (95% CI)		1.4588 (0.8212, 2.5916)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1978
Odds Ratio (OR) (95% CI)		1.5342 (0.8009, 2.9393)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1969
Risk Difference (RD) (95% CI)		0.0444 (-0.0230, 0.1118)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1967
Subjects with non-severe events (Maximum Grade 1/2)	18 (9.68)	23 (13.53)
Relative Risk (RR) (95% CI)		1.3980 (0.7822, 2.4986)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2581
Odds Ratio (OR) (95% CI)		1.4603 (0.7583, 2.8122)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2574

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Risk Difference (RD) (95% CI)		0.0385 (-0.0282, 0.1052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2577
Subjects with severe events (Maximum Grade 3/4/5)	0	1 (0.59)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.7.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Cataract Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any Treatment-emergent Cataract Events	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.8.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Cataract Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with non-severe events (Maximum Grade 1/2)	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.8.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Cataract Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with severe events (Maximum Grade 3/4/5)	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.8.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Cataract Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with serious events	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with any Treatment-emergent Cataract Events	0	1 (0.65)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	0	1 (0.65)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with any Treatment-emergent Cataract Events	4 (3.36)	1 (0.80)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	4 (3.36)	1 (0.80)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with any Treatment-emergent Cataract Events	4 (10.53)	1 (2.44)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	4 (10.53)	1 (2.44)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with any Treatment-emergent Cataract Events	0	2 (0.82)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	0	2 (0.82)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with any Treatment-emergent Cataract Events	1 (1.25)	2 (2.78)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	1 (1.25)	2 (2.78)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with any Treatment-emergent Cataract Events	3 (1.49)	1 (0.48)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	3 (1.49)	1 (0.48)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with any Treatment-emergent Cataract Events	2 (1.39)	1 (0.67)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	2 (1.39)	1 (0.67)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with any Treatment-emergent Cataract Events	2 (1.38)	2 (1.48)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	2 (1.38)	2 (1.48)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with any Treatment-emergent Cataract Events	3 (2.91)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	3 (2.91)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any Treatment-emergent Cataract Events	1 (0.54)	3 (1.76)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	1 (0.54)	3 (1.76)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.8.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Hypoglycemia Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any Treatment-emergent Hypoglycemia Events	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.6432
Age at screening (<18 years vs. ≥18 years)	>0.9999
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.1534

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.9.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Hypoglycemia Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with non-severe events (Maximum Grade 1/2)	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.6432
Age at screening (<18 years vs. ≥18 years)	>0.9999
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.1534

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.9.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Hypoglycemia Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with severe events (Maximum Grade 3/4/5)	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.9.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Hypoglycemia Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with serious events	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	9 (5.39)	2 (1.30)
Relative Risk (RR) (95% CI)		0.2410 (0.0529, 1.0979)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0659
Odds Ratio (OR) (95% CI)		0.2310 (0.0491, 1.0864)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0636
Risk Difference (RD) (95% CI)		-0.0409 (-0.0795, -0.0023)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0380
Subjects with non-severe events (Maximum Grade 1/2)	9 (5.39)	2 (1.30)
Relative Risk (RR) (95% CI)		0.2410 (0.0529, 1.0979)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0659
Odds Ratio (OR) (95% CI)		0.2310 (0.0491, 1.0864)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0636

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Risk Difference (RD) (95% CI)		-0.0409 (-0.0795, -0.0023)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0380
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	2 (1.68)	1 (0.80)
Relative Risk (RR) (95% CI)		0.4760 (0.0437, 5.1808)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5422
Odds Ratio (OR) (95% CI)		0.4718 (0.0422, 5.2722)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5418
Risk Difference (RD) (95% CI)		-0.0088 (-0.0367, 0.0191)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5358
Subjects with non-severe events (Maximum Grade 1/2)	2 (1.68)	1 (0.80)
Relative Risk (RR) (95% CI)		0.4760 (0.0437, 5.1808)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5422
Odds Ratio (OR) (95% CI)		0.4718 (0.0422, 5.2722)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5418

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Risk Difference (RD) (95% CI)		-0.0088 (-0.0367, 0.0191)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5358
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	11 (4.38)	3 (1.23)
Relative Risk (RR) (95% CI)		0.2817 (0.0796, 0.9975)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0495
Odds Ratio (OR) (95% CI)		0.2727 (0.0751, 0.9898)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0482
Risk Difference (RD) (95% CI)		-0.0315 (-0.0604, -0.0026)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0327
Subjects with non-severe events (Maximum Grade 1/2)	11 (4.38)	3 (1.23)
Relative Risk (RR) (95% CI)		0.2817 (0.0796, 0.9975)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0495
Odds Ratio (OR) (95% CI)		0.2727 (0.0751, 0.9898)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0482

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Risk Difference (RD) (95% CI)		-0.0315 (-0.0604, -0.0026)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0327
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	2 (2.50)	2 (2.78)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	2 (2.50)	2 (2.78)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	8 (3.96)	1 (0.48)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	8 (3.96)	1 (0.48)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	7 (4.86)	2 (1.34)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	7 (4.86)	2 (1.34)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	4 (2.76)	1 (0.74)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with non-severe events (Maximum Grade 1/2)	4 (2.76)	1 (0.74)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	7 (6.80)	3 (2.63)
Relative Risk (RR) (95% CI)		0.3872 (0.1028, 1.4582)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1608
Odds Ratio (OR) (95% CI)		0.3707 (0.0933, 1.4730)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1586
Risk Difference (RD) (95% CI)		-0.0416 (-0.0984, 0.0152)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1507
Subjects with non-severe events (Maximum Grade 1/2)	7 (6.80)	3 (2.63)
Relative Risk (RR) (95% CI)		0.3872 (0.1028, 1.4582)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1608
Odds Ratio (OR) (95% CI)		0.3707 (0.0933, 1.4730)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1586

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Risk Difference (RD) (95% CI)		-0.0416 (-0.0984, 0.0152)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1507
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	4 (2.15)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0215 (-0.0424, -0.0007)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0432
Subjects with non-severe events (Maximum Grade 1/2)	4 (2.15)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Risk Difference (RD) (95% CI)		-0.0215 (-0.0424, -0.0007)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0432
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.9.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Neuropsychiatric Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any Treatment-emergent Neuropsychiatric Events	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	0.1750
Age at screening (<18 years vs. ≥18 years)	0.1846
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.1759
Sex (Male vs. Female)	0.8399
Region (North America vs. Rest of the World)	0.3152

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.10.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Neuropsychiatric Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with non-severe events (Maximum Grade 1/2)	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.2903
Age at screening (<18 years vs. ≥18 years)	>0.9999
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.1925
Sex (Male vs. Female)	0.7052
Region (North America vs. Rest of the World)	0.2494

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.10.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Neuropsychiatric Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with severe events (Maximum Grade 3/4/5)	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.10.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for AESI of Treatment-emergent Neuropsychiatric Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with serious events	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	-
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	20 (11.98)	17 (11.04)
Relative Risk (RR) (95% CI)		0.9218 (0.5017, 1.6936)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7929
Odds Ratio (OR) (95% CI)		0.9120 (0.4588, 1.8132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7929
Risk Difference (RD) (95% CI)		-0.0094 (-0.0792, 0.0604)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7925
Subjects with non-severe events (Maximum Grade 1/2)	18 (10.78)	17 (11.04)
Relative Risk (RR) (95% CI)		1.0242 (0.5478, 1.9146)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9404
Odds Ratio (OR) (95% CI)		1.0272 (0.5089, 2.0732)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9404

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Risk Difference (RD) (95% CI)		0.0026 (-0.0657, 0.0709)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9404
Subjects with severe events (Maximum Grade 3/4/5)	2 (1.20)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	1 (0.60)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	11 (9.24)	20 (16.00)
Relative Risk (RR) (95% CI)		1.7309 (0.8668, 3.4564)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1200
Odds Ratio (OR) (95% CI)		1.8701 (0.8545, 4.0928)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1172
Risk Difference (RD) (95% CI)		0.0676 (-0.0151, 0.1503)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1093
Subjects with non-severe events (Maximum Grade 1/2)	10 (8.40)	18 (14.40)
Relative Risk (RR) (95% CI)		1.7136 (0.8249, 3.5599)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1488
Odds Ratio (OR) (95% CI)		1.8336 (0.8094, 4.1539)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1462

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- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Risk Difference (RD) (95% CI)		0.0600 (-0.0192, 0.1392)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1378
Subjects with severe events (Maximum Grade 3/4/5)	1 (0.84)	2 (1.60)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	1 (0.84)	1 (0.80)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	1 (2.63)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0263 (-0.0772, 0.0246)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3109
Subjects with non-severe events (Maximum Grade 1/2)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with severe events (Maximum Grade 3/4/5)	1 (2.63)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	1 (2.63)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	30 (11.95)	38 (15.64)
Relative Risk (RR) (95% CI)		1.3084 (0.8384, 2.0417)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2365
Odds Ratio (OR) (95% CI)		1.3655 (0.8159, 2.2855)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2358
Risk Difference (RD) (95% CI)		0.0369 (-0.0239, 0.0977)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2348
Subjects with non-severe events (Maximum Grade 1/2)	28 (11.16)	36 (14.81)
Relative Risk (RR) (95% CI)		1.3280 (0.8373, 2.1064)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2280
Odds Ratio (OR) (95% CI)		1.3851 (0.8162, 2.3505)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2273

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Risk Difference (RD) (95% CI)		0.0366 (-0.0227, 0.0959)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2262
Subjects with severe events (Maximum Grade 3/4/5)	2 (0.80)	2 (0.82)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	1 (0.40)	1 (0.41)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	8 (10.00)	14 (19.44)
Relative Risk (RR) (95% CI)		1.9444 (0.8666, 4.3631)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1068
Odds Ratio (OR) (95% CI)		2.1724 (0.8529, 5.5334)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1039
Risk Difference (RD) (95% CI)		0.0944 (-0.0182, 0.2070)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1002
Subjects with non-severe events (Maximum Grade 1/2)	7 (8.75)	13 (18.06)
Relative Risk (RR) (95% CI)		2.0635 (0.8715, 4.8857)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0995
Odds Ratio (OR) (95% CI)		2.2978 (0.8617, 6.1275)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0964

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Risk Difference (RD) (95% CI)		0.0931 (-0.0152, 0.2014)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0922
Subjects with severe events (Maximum Grade 3/4/5)	1 (1.25)	1 (1.39)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	1 (1.25)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	23 (11.39)	24 (11.43)
Relative Risk (RR) (95% CI)		1.0037 (0.5859, 1.7195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9892
Odds Ratio (OR) (95% CI)		1.0042 (0.5469, 1.8438)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9892
Risk Difference (RD) (95% CI)		0.0004 (-0.0610, 0.0618)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9892
Subjects with non-severe events (Maximum Grade 1/2)	21 (10.40)	23 (10.95)
Relative Risk (RR) (95% CI)		1.0535 (0.6023, 1.8428)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8550
Odds Ratio (OR) (95% CI)		1.0601 (0.5669, 1.9822)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8550

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Risk Difference (RD) (95% CI)		0.0056 (-0.0541, 0.0652)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8549
Subjects with severe events (Maximum Grade 3/4/5)	2 (0.99)	1 (0.48)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	1 (0.50)	1 (0.48)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	10 (6.94)	14 (9.40)
Relative Risk (RR) (95% CI)		1.3530 (0.6212, 2.9472)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4466
Odds Ratio (OR) (95% CI)		1.3896 (0.5963, 3.2382)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4459
Risk Difference (RD) (95% CI)		0.0245 (-0.0381, 0.0871)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4427
Subjects with non-severe events (Maximum Grade 1/2)	9 (6.25)	14 (9.40)
Relative Risk (RR) (95% CI)		1.5034 (0.6718, 3.3641)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3212
Odds Ratio (OR) (95% CI)		1.5556 (0.6512, 3.7156)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3199

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Risk Difference (RD) (95% CI)		0.0315 (-0.0298, 0.0928)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3145
Subjects with severe events (Maximum Grade 3/4/5)	1 (0.69)	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	21 (14.48)	24 (17.78)
Relative Risk (RR) (95% CI)		1.2275 (0.7177, 2.0995)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4541
Odds Ratio (OR) (95% CI)		1.2767 (0.6737, 2.4193)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4538
Risk Difference (RD) (95% CI)		0.0330 (-0.0533, 0.1192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4540
Subjects with non-severe events (Maximum Grade 1/2)	19 (13.10)	22 (16.30)
Relative Risk (RR) (95% CI)		1.2437 (0.7052, 2.1932)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4512
Odds Ratio (OR) (95% CI)		1.2911 (0.6645, 2.5087)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4509

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Risk Difference (RD) (95% CI)		0.0319 (-0.0511, 0.1150)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4512
Subjects with severe events (Maximum Grade 3/4/5)	2 (1.38)	2 (1.48)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	2 (1.38)	1 (0.74)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	11 (10.68)	11 (9.65)
Relative Risk (RR) (95% CI)		0.9035 (0.4092, 1.9950)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8018
Odds Ratio (OR) (95% CI)		0.8932 (0.3698, 2.1572)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8018
Risk Difference (RD) (95% CI)		-0.0103 (-0.0909, 0.0703)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8021
Subjects with non-severe events (Maximum Grade 1/2)	11 (10.68)	11 (9.65)
Relative Risk (RR) (95% CI)		0.9035 (0.4092, 1.9950)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8018
Odds Ratio (OR) (95% CI)		0.8932 (0.3698, 2.1572)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8018

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Risk Difference (RD) (95% CI)		-0.0103 (-0.0909, 0.0703)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8021
Subjects with severe events (Maximum Grade 3/4/5)	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	20 (10.75)	27 (15.88)
Relative Risk (RR) (95% CI)		1.4771 (0.8612, 2.5335)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1565
Odds Ratio (OR) (95% CI)		1.5671 (0.8431, 2.9131)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1555
Risk Difference (RD) (95% CI)		0.0513 (-0.0194, 0.1220)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1551
Subjects with non-severe events (Maximum Grade 1/2)	17 (9.14)	25 (14.71)
Relative Risk (RR) (95% CI)		1.6090 (0.9009, 2.8737)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1080
Odds Ratio (OR) (95% CI)		1.7140 (0.8904, 3.2992)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1068

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Risk Difference (RD) (95% CI)		0.0557 (-0.0118, 0.1231)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1058
Subjects with severe events (Maximum Grade 3/4/5)	3 (1.61)	2 (1.18)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Subjects with serious events	2 (1.08)	1 (0.59)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.10.2
Study VX20-121-103: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.11.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Death
Safety Set

	P-value for Interaction Based on Relative Risk

No data met the criteria for this table.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.11.2
Study VX20-121-103: Summary of Death by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.11.2
Study VX20-121-103: Summary of Death by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.11.2
Study VX20-121-103: Summary of Death by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.11.2
Study VX20-121-103: Summary of Death by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.11.2
Study VX20-121-103: Summary of Death by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.11.2
Study VX20-121-103: Summary of Death by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.11.2
Study VX20-121-103: Summary of Death by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.11.2
Study VX20-121-103: Summary of Death by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.11.2
Study VX20-121-103: Summary of Death by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.11.2
Study VX20-121-103: Summary of Death by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.12.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Treatment-emergent Infective Pulmonary Exacerbation Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.5716
Age at screening (<18 years vs. ≥18 years)	0.2023
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.7263
Sex (Male vs. Female)	0.9732
Region (North America vs. Rest of the World)	0.6468

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.12.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Treatment-emergent Infective Pulmonary Exacerbation Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with non-severe events (Maximum Grade 1/2)	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.8806
Age at screening (<18 years vs. ≥18 years)	0.7826
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.3574
Sex (Male vs. Female)	0.7307
Region (North America vs. Rest of the World)	0.6243

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.12.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Treatment-emergent Infective Pulmonary Exacerbation Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with severe events (Maximum Grade 3/4/5)	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.1688
Age at screening (<18 years vs. ≥18 years)	0.2066
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.3262
Sex (Male vs. Female)	0.9169
Region (North America vs. Rest of the World)	0.6956

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.12.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Treatment-emergent Infective Pulmonary Exacerbation Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with serious events	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.6558
Age at screening (<18 years vs. ≥18 years)	0.1946
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.7270
Sex (Male vs. Female)	0.5562
Region (North America vs. Rest of the World)	0.2912

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	62 (37.13)	48 (31.17)
Relative Risk (RR) (95% CI)		0.8395 (0.6178, 1.1408)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2637
Odds Ratio (OR) (95% CI)		0.7669 (0.4824, 1.2190)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2617
Risk Difference (RD) (95% CI)		-0.0596 (-0.1631, 0.0440)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2595
Subjects with non-severe events (Maximum Grade 1/2)	56 (33.53)	43 (27.92)
Relative Risk (RR) (95% CI)		0.8327 (0.5976, 1.1601)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2792
Odds Ratio (OR) (95% CI)		0.7679 (0.4768, 1.2367)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2774

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Risk Difference (RD) (95% CI)		-0.0561 (-0.1568, 0.0446)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2750
Subjects with severe events (Maximum Grade 3/4/5)	6 (3.59)	5 (3.25)
Relative Risk (RR) (95% CI)		0.9037 (0.2815, 2.9013)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8649
Odds Ratio (OR) (95% CI)		0.9004 (0.2692, 3.0122)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8649
Risk Difference (RD) (95% CI)		-0.0035 (-0.0432, 0.0363)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8645
Subjects with serious events	9 (5.39)	11 (7.14)
Relative Risk (RR) (95% CI)		1.3254 (0.5646, 3.1112)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5176

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Odds Ratio (OR) (95% CI)		1.3504 (0.5438, 3.3533)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5174
Risk Difference (RD) (95% CI)		0.0175 (-0.0356, 0.0707)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5180

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	26 (21.85)	27 (21.60)
Relative Risk (RR) (95% CI)		0.9886 (0.6139, 1.5920)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9624
Odds Ratio (OR) (95% CI)		0.9855 (0.5362, 1.8114)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9624
Risk Difference (RD) (95% CI)		-0.0025 (-0.1060, 0.1010)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9624
Subjects with non-severe events (Maximum Grade 1/2)	24 (20.17)	20 (16.00)
Relative Risk (RR) (95% CI)		0.7933 (0.4634, 1.3582)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3987
Odds Ratio (OR) (95% CI)		0.7540 (0.3916, 1.4516)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3982

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Risk Difference (RD) (95% CI)		-0.0417 (-0.1383, 0.0549)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3976
Subjects with severe events (Maximum Grade 3/4/5)	2 (1.68)	7 (5.60)
Relative Risk (RR) (95% CI)		3.3320 (0.7063, 15.7189)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1283
Odds Ratio (OR) (95% CI)		3.4703 (0.7062, 17.0541)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1256
Risk Difference (RD) (95% CI)		0.0392 (-0.0073, 0.0856)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0982
Subjects with serious events	3 (2.52)	6 (4.80)
Relative Risk (RR) (95% CI)		1.9040 (0.4872, 7.4405)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3544

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

ppFEV$_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Odds Ratio (OR) (95% CI)		1.9496 (0.4763, 7.9798)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3532
Risk Difference (RD) (95% CI)		0.0228 (-0.0241, 0.0697)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3407

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- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	7 (18.42)	11 (26.83)
Relative Risk (RR) (95% CI)		1.4564 (0.6297, 3.3689)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3795
Odds Ratio (OR) (95% CI)		1.6238 (0.5557, 4.7452)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3756
Risk Difference (RD) (95% CI)		0.0841 (-0.0992, 0.2673)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3685
Subjects with non-severe events (Maximum Grade 1/2)	6 (15.79)	6 (14.63)
Relative Risk (RR) (95% CI)		0.9268 (0.3269, 2.6274)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8863
Odds Ratio (OR) (95% CI)		0.9143 (0.2675, 3.1247)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8864

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Risk Difference (RD) (95% CI)		-0.0116 (-0.1701, 0.1470)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8865
Subjects with severe events (Maximum Grade 3/4/5)	1 (2.63)	5 (12.20)
Relative Risk (RR) (95% CI)		4.6341 (0.5668, 37.8880)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1526
Odds Ratio (OR) (95% CI)		5.1389 (0.5720, 46.1709)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1440
Risk Difference (RD) (95% CI)		0.0956 (-0.0167, 0.2080)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0952
Subjects with serious events	1 (2.63)	5 (12.20)
Relative Risk (RR) (95% CI)		4.6341 (0.5668, 37.8880)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1526

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Odds Ratio (OR) (95% CI)		5.1389 (0.5720, 46.1709)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1440
Risk Difference (RD) (95% CI)		0.0956 (-0.0167, 0.2080)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0952

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	81 (32.27)	65 (26.75)
Relative Risk (RR) (95% CI)		0.8289 (0.6298, 1.0908)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1804
Odds Ratio (OR) (95% CI)		0.7664 (0.5198, 1.1299)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1792
Risk Difference (RD) (95% CI)		-0.0552 (-0.1355, 0.0250)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1775
Subjects with non-severe events (Maximum Grade 1/2)	74 (29.48)	57 (23.46)
Relative Risk (RR) (95% CI)		0.7956 (0.5912, 1.0707)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1313
Odds Ratio (OR) (95% CI)		0.7330 (0.4903, 1.0958)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1300

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Risk Difference (RD) (95% CI)		-0.0603 (-0.1378, 0.0173)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1280
Subjects with severe events (Maximum Grade 3/4/5)	7 (2.79)	8 (3.29)
Relative Risk (RR) (95% CI)		1.1805 (0.4347, 3.2054)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7448
Odds Ratio (OR) (95% CI)		1.1866 (0.4236, 3.3241)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7447
Risk Difference (RD) (95% CI)		0.0050 (-0.0253, 0.0353)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7448
Subjects with serious events	11 (4.38)	13 (5.35)
Relative Risk (RR) (95% CI)		1.2207 (0.5577, 2.6719)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6178

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Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Odds Ratio (OR) (95% CI)		1.2332 (0.5415, 2.8086)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6177
Risk Difference (RD) (95% CI)		0.0097 (-0.0283, 0.0476)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6176

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Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	26 (32.50)	22 (30.56)
Relative Risk (RR) (95% CI)		0.9402 (0.5876, 1.5044)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7970
Odds Ratio (OR) (95% CI)		0.9138 (0.4603, 1.8143)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7968
Risk Difference (RD) (95% CI)		-0.0194 (-0.1673, 0.1284)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7966
Subjects with non-severe events (Maximum Grade 1/2)	24 (30.00)	21 (29.17)
Relative Risk (RR) (95% CI)		0.9722 (0.5947, 1.5894)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9106
Odds Ratio (OR) (95% CI)		0.9608 (0.4782, 1.9305)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9105

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Risk Difference (RD) (95% CI)		-0.0083 (-0.1536, 0.1369)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9105
Subjects with severe events (Maximum Grade 3/4/5)	2 (2.50)	1 (1.39)
Relative Risk (RR) (95% CI)		0.5556 (0.0515, 5.9982)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6282
Odds Ratio (OR) (95% CI)		0.5493 (0.0488, 6.1890)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6278
Risk Difference (RD) (95% CI)		-0.0111 (-0.0547, 0.0325)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6175
Subjects with serious events	3 (3.75)	5 (6.94)
Relative Risk (RR) (95% CI)		1.8519 (0.4587, 7.4759)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3868

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Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Odds Ratio (OR) (95% CI)		1.9154 (0.4411, 8.3168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3856
Risk Difference (RD) (95% CI)		0.0319 (-0.0400, 0.1039)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3844

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	60 (29.70)	53 (25.24)
Relative Risk (RR) (95% CI)		0.8497 (0.6201, 1.1642)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3107
Odds Ratio (OR) (95% CI)		0.7989 (0.5178, 1.2326)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3103
Risk Difference (RD) (95% CI)		-0.0446 (-0.1308, 0.0415)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3097
Subjects with non-severe events (Maximum Grade 1/2)	54 (26.73)	41 (19.52)
Relative Risk (RR) (95% CI)		0.7303 (0.5110, 1.0438)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0846
Odds Ratio (OR) (95% CI)		0.6649 (0.4189, 1.0555)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0835

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Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Risk Difference (RD) (95% CI)		-0.0721 (-0.1533, 0.0091)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0820
Subjects with severe events (Maximum Grade 3/4/5)	6 (2.97)	12 (5.71)
Relative Risk (RR) (95% CI)		1.9238 (0.7361, 5.0282)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1819
Odds Ratio (OR) (95% CI)		1.9798 (0.7286, 5.3799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1805
Risk Difference (RD) (95% CI)		0.0274 (-0.0117, 0.0666)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1697
Subjects with serious events	9 (4.46)	13 (6.19)
Relative Risk (RR) (95% CI)		1.3894 (0.6073, 3.1789)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4361

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Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Odds Ratio (OR) (95% CI)		1.4151 (0.5912, 3.3871)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4356
Risk Difference (RD) (95% CI)		0.0174 (-0.0259, 0.0606)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4319

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Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	35 (24.31)	32 (21.48)
Relative Risk (RR) (95% CI)		0.8836 (0.5799, 1.3463)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5647
Odds Ratio (OR) (95% CI)		0.8518 (0.4935, 1.4701)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5645
Risk Difference (RD) (95% CI)		-0.0283 (-0.1245, 0.0679)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5644
Subjects with non-severe events (Maximum Grade 1/2)	34 (23.61)	30 (20.13)
Relative Risk (RR) (95% CI)		0.8527 (0.5524, 1.3165)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4722
Odds Ratio (OR) (95% CI)		0.8156 (0.4681, 1.4210)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4718

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
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Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Risk Difference (RD) (95% CI)		-0.0348 (-0.1294, 0.0599)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4715
Subjects with severe events (Maximum Grade 3/4/5)	1 (0.69)	2 (1.34)
Relative Risk (RR) (95% CI)		1.9329 (0.1772, 21.0841)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5888
Odds Ratio (OR) (95% CI)		1.9456 (0.1745, 21.6938)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5885
Risk Difference (RD) (95% CI)		0.0065 (-0.0164, 0.0294)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5796
Subjects with serious events	1 (0.69)	3 (2.01)
Relative Risk (RR) (95% CI)		2.8993 (0.3051, 27.5508)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3541

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Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Odds Ratio (OR) (95% CI)		2.9384 (0.3021, 28.5809)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3531
Risk Difference (RD) (95% CI)		0.0132 (-0.0131, 0.0395)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3260

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Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	53 (36.55)	44 (32.59)
Relative Risk (RR) (95% CI)		0.8917 (0.6450, 1.2326)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4877
Odds Ratio (OR) (95% CI)		0.8393 (0.5123, 1.3751)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4868
Risk Difference (RD) (95% CI)		-0.0396 (-0.1509, 0.0717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4858
Subjects with non-severe events (Maximum Grade 1/2)	46 (31.72)	33 (24.44)
Relative Risk (RR) (95% CI)		0.7705 (0.5265, 1.1276)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1796
Odds Ratio (OR) (95% CI)		0.6963 (0.4116, 1.1779)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1772

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- [2] Odds ratio from 2x2 table.
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Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Risk Difference (RD) (95% CI)		-0.0728 (-0.1776, 0.0321)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1736
Subjects with severe events (Maximum Grade 3/4/5)	7 (4.83)	11 (8.15)
Relative Risk (RR) (95% CI)		1.6878 (0.6739, 4.2276)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2638
Odds Ratio (OR) (95% CI)		1.7488 (0.6576, 4.6512)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2627
Risk Difference (RD) (95% CI)		0.0332 (-0.0246, 0.0911)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2606
Subjects with serious events	11 (7.59)	15 (11.11)
Relative Risk (RR) (95% CI)		1.4646 (0.6975, 3.0756)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3134

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Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Odds Ratio (OR) (95% CI)		1.5227 (0.6733, 3.4439)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3125
Risk Difference (RD) (95% CI)		0.0352 (-0.0331, 0.1036)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3119

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- [1] Relative risk from 2x2 table.
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Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	30 (29.13)	27 (23.68)
Relative Risk (RR) (95% CI)		0.8132 (0.5203, 1.2708)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3639
Odds Ratio (OR) (95% CI)		0.7552 (0.4120, 1.3841)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3637
Risk Difference (RD) (95% CI)		-0.0544 (-0.1718, 0.0630)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3637
Subjects with non-severe events (Maximum Grade 1/2)	26 (25.24)	21 (18.42)
Relative Risk (RR) (95% CI)		0.7298 (0.4384, 1.2148)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2256
Odds Ratio (OR) (95% CI)		0.6687 (0.3493, 1.2804)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2247

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Risk Difference (RD) (95% CI)		-0.0682 (-0.1782, 0.0418)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2242
Subjects with severe events (Maximum Grade 3/4/5)	4 (3.88)	6 (5.26)
Relative Risk (RR) (95% CI)		1.3553 (0.3935, 4.6682)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6300
Odds Ratio (OR) (95% CI)		1.3750 (0.3769, 5.0162)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6296
Risk Difference (RD) (95% CI)		0.0138 (-0.0416, 0.0692)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6257
Subjects with serious events	5 (4.85)	5 (4.39)
Relative Risk (RR) (95% CI)		0.9035 (0.2693, 3.0318)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8695

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Odds Ratio (OR) (95% CI)		0.8991 (0.2527, 3.1991)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8695
Risk Difference (RD) (95% CI)		-0.0047 (-0.0607, 0.0513)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8698

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- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	58 (31.18)	49 (28.82)
Relative Risk (RR) (95% CI)		0.9243 (0.6723, 1.2709)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6282
Odds Ratio (OR) (95% CI)		0.8937 (0.5674, 1.4076)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6278
Risk Difference (RD) (95% CI)		-0.0236 (-0.1188, 0.0716)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6273
Subjects with non-severe events (Maximum Grade 1/2)	54 (29.03)	42 (24.71)
Relative Risk (RR) (95% CI)		0.8510 (0.6024, 1.2021)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3599
Odds Ratio (OR) (95% CI)		0.8021 (0.5009, 1.2844)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3586

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Risk Difference (RD) (95% CI)		-0.0433 (-0.1352, 0.0487)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3565
Subjects with severe events (Maximum Grade 3/4/5)	4 (2.15)	7 (4.12)
Relative Risk (RR) (95% CI)		1.9147 (0.5705, 6.4257)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2930
Odds Ratio (OR) (95% CI)		1.9540 (0.5618, 6.7964)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2922
Risk Difference (RD) (95% CI)		0.0197 (-0.0168, 0.0561)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2898
Subjects with serious events	7 (3.76)	13 (7.65)
Relative Risk (RR) (95% CI)		2.0319 (0.8303, 4.9728)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1205

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.12.2
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Odds Ratio (OR) (95% CI)		2.1174 (0.8242, 5.4395)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1191
Risk Difference (RD) (95% CI)		0.0388 (-0.0096, 0.0872)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1159

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.4.1.1
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with at least one Pulmonary Exacerbation	59 (20.42)	61 (21.48)
Relative Risk (RR) (95% CI)		1.0421 (0.7576, 1.4335)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7997
Odds Ratio (OR) (95% CI)		1.0729 (0.7123, 1.6160)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.7364
Risk Difference (RD) (95% CI)		0.0200 (-0.0476, 0.0875)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.5629
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	9 (3.11)	14 (4.93)
Relative Risk (RR) (95% CI)		1.4298 (0.6225, 3.2840)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3994
Odds Ratio (OR) (95% CI)		1.4430 (0.6047, 3.4435)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4085
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 2.4.1.1
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	17 (5.88)	19 (6.69)
Relative Risk (RR) (95% CI)		1.0957 (0.5714, 2.1011)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7833
Odds Ratio (OR) (95% CI)		1.1063 (0.5495, 2.2272)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.7772
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 2.4.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

Subgroup	P-value for Interaction
Subjects with at least one Pulmonary Exacerbation	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %) [1]	0.3812
Age at screening (<18 years vs. ≥18 years) [2]	0.4488
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.4100
Sex (Male vs. Female) [1]	0.7623
Region (North America vs. Rest of the World) [1]	0.9533
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %) [1]	0.4064
Age at screening (<18 years vs. ≥18 years) [2]	0.2533
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.1719
Sex (Male vs. Female) [1]	0.4874
Region (North America vs. Rest of the World) [1]	0.4995

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, age at screening (<18 vs ≥18 years), genotype and treatment*subgroup, with adjustment for continuous baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, genotype, treatment*subgroup, with adjustment for continuous baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 2.4.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

Subgroup	P-value for Interaction
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1630
Age at screening (<18 years vs. ≥18 years) [2]	0.1456
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.7572
Sex (Male vs. Female) [1]	0.8599
Region (North America vs. Rest of the World) [1]	0.2377

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, age at screening (<18 vs ≥18 years), genotype and treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, genotype, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at Baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with at least one Pulmonary Exacerbation	41 (24.55)	36 (23.38)
Relative Risk (RR) (95% CI)		0.9396 (0.6345, 1.3915)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7559
Odds Ratio (OR) (95% CI)		0.9239 (0.5497, 1.5528)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.7651
Risk Difference (RD) (95% CI)		-0.0131 (-0.1085, 0.0823)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.7885
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	6 (3.59)	6 (3.90)
Relative Risk (RR) (95% CI)		1.0430 (0.3467, 3.1374)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.9403
Odds Ratio (OR) (95% CI)		1.0666 (0.3307, 3.4395)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.9141
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at Baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	13 (7.78)	9 (5.84)
Relative Risk (RR) (95% CI)		0.7915 (0.3447, 1.8172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.5813
Odds Ratio (OR) (95% CI)		0.7739 (0.3139, 1.9078)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.5777
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at Baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with at least one Pulmonary Exacerbation	18 (15.13)	24 (19.20)
Relative Risk (RR) (95% CI)		1.2391 (0.7112, 2.1587)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4491
Odds Ratio (OR) (95% CI)		1.3199 (0.6676, 2.6097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4249
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	3 (2.52)	7 (5.60)
Relative Risk (RR) (95% CI)		2.0925 (0.5518, 7.9348)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2776
Odds Ratio (OR) (95% CI)		2.1341 (0.5297, 8.5988)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2864
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

ppFEV$_1$ at Baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	4 (3.36)	9 (7.20)
Relative Risk (RR) (95% CI)		2.0261 (0.6379, 6.4355)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2311
Odds Ratio (OR) (95% CI)		2.1088 (0.6203, 7.1689)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2320
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with at least one Pulmonary Exacerbation	4 (10.53)	8 (19.51)
Relative Risk (RR) (95% CI)		1.8208 (0.5707, 5.8093)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3114
Odds Ratio (OR) (95% CI)		1.8972 (0.4747, 7.5820)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.3650
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	1 (2.63)	5 (12.20)
Relative Risk (RR) (95% CI)		10.3008 (3.8450, 27.5958)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	<0.0001*
Odds Ratio (OR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	N/C
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	1 (2.63)	5 (12.20)
Relative Risk (RR) (95% CI)		10.3008 (3.8450, 27.5958)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	<0.0001*
Odds Ratio (OR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	N/C
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with at least one Pulmonary Exacerbation	55 (21.91)	53 (21.81)
Relative Risk (RR) (95% CI)		1.0057 (0.7204, 1.4041)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.9734
Odds Ratio (OR) (95% CI)		1.0268 (0.6660, 1.5830)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.9046
Risk Difference (RD) (95% CI)		0.0155 (-0.0607, 0.0916)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.6903
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	8 (3.19)	9 (3.70)
Relative Risk (RR) (95% CI)		1.1322 (0.4440, 2.8873)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7948
Odds Ratio (OR) (95% CI)		1.1383 (0.4299, 3.0139)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.7943
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

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Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	16 (6.37)	14 (5.76)
Relative Risk (RR) (95% CI)		0.9172 (0.4525, 1.8591)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.8104
Odds Ratio (OR) (95% CI)		0.9138 (0.4286, 1.9482)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.8154
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with at least one Pulmonary Exacerbation	21 (26.25)	15 (20.83)
Relative Risk (RR) (95% CI)		0.8491 (0.4810, 1.4988)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.5726
Odds Ratio (OR) (95% CI)		0.7889 (0.3613, 1.7224)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.5517
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	4 (5.00)	2 (2.78)
Relative Risk (RR) (95% CI)		0.4771 (0.1001, 2.2743)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3530*
Odds Ratio (OR) (95% CI)		0.4976 (0.0819, 3.0241)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4484
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

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Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	4 (5.00)	3 (4.17)
Relative Risk (RR) (95% CI)		0.7580 (0.1787, 3.2159)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7071*
Odds Ratio (OR) (95% CI)		0.8031 (0.1593, 4.0484)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.7905
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

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Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with at least one Pulmonary Exacerbation	37 (18.32)	46 (21.90)
Relative Risk (RR) (95% CI)		1.1697 (0.7904, 1.7310)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4332
Odds Ratio (OR) (95% CI)		1.2220 (0.7499, 1.9913)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4210
Risk Difference (RD) (95% CI)		0.0397 (-0.0392, 0.1185)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.3243
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	5 (2.48)	12 (5.71)
Relative Risk (RR) (95% CI)		2.0766 (0.7383, 5.8406)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1661
Odds Ratio (OR) (95% CI)		2.1595 (0.7297, 6.3909)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.1643
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

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Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	12 (5.94)	16 (7.62)
Relative Risk (RR) (95% CI)		1.1588 (0.5568, 2.4117)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6936
Odds Ratio (OR) (95% CI)		1.1770 (0.5339, 2.5948)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6862
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with at least one Pulmonary Exacerbation	23 (15.97)	25 (16.78)
Relative Risk (RR) (95% CI)		1.0278 (0.6040, 1.7490)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.9194
Odds Ratio (OR) (95% CI)		1.0445 (0.5522, 1.9756)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.8936
Risk Difference (RD) (95% CI)		0.0185 (-0.0732, 0.1103)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.6924
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	2 (1.39)	5 (3.36)
Relative Risk (RR) (95% CI)		2.3871 (0.4680, 12.1752)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2952
Odds Ratio (OR) (95% CI)		2.4196 (0.4513, 12.9732)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.3024
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

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Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	5 (3.47)	5 (3.36)
Relative Risk (RR) (95% CI)		1.1178 (0.3029, 4.1252)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.8672
Odds Ratio (OR) (95% CI)		1.1097 (0.2861, 4.3040)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.8804
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with at least one Pulmonary Exacerbation	36 (24.83)	36 (26.67)
Relative Risk (RR) (95% CI)		1.1186 (0.7487, 1.6714)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.5843
Odds Ratio (OR) (95% CI)		1.1929 (0.6843, 2.0794)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.5339
Risk Difference (RD) (95% CI)		0.0297 (-0.0710, 0.1304)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.5629
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	7 (4.83)	9 (6.67)
Relative Risk (RR) (95% CI)		1.1792 (0.4349, 3.1972)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7460
Odds Ratio (OR) (95% CI)		1.2104 (0.4180, 3.5052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.7249
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	12 (8.28)	14 (10.37)
Relative Risk (RR) (95% CI)		1.2072 (0.5556, 2.6234)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6344*
Odds Ratio (OR) (95% CI)		1.2452 (0.5356, 2.8951)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6105
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with at least one Pulmonary Exacerbation	21 (20.39)	26 (22.81)
Relative Risk (RR) (95% CI)		1.0113 (0.6059, 1.6880)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.9656
Odds Ratio (OR) (95% CI)		1.0219 (0.5271, 1.9809)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.9489
Risk Difference (RD) (95% CI)		0.0137 (-0.0993, 0.1267)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.8120
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	3 (2.91)	8 (7.02)
Relative Risk (RR) (95% CI)		2.1088 (0.5607, 7.9310)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2696
Odds Ratio (OR) (95% CI)		2.1331 (0.5226, 8.7061)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2911
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	4 (3.88)	10 (8.77)
Relative Risk (RR) (95% CI)		1.9601 (0.6268, 6.1296)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2473
Odds Ratio (OR) (95% CI)		2.0108 (0.5866, 6.8932)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2665
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with at least one Pulmonary Exacerbation	38 (20.43)	35 (20.59)
Relative Risk (RR) (95% CI)		1.0500 (0.6981, 1.5793)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.8147
Odds Ratio (OR) (95% CI)		1.0809 (0.6387, 1.8292)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.7720
Risk Difference (RD) (95% CI)		0.0220 (-0.0638, 0.1077)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.6155
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	6 (3.23)	6 (3.53)
Relative Risk (RR) (95% CI)		1.1019 (0.3640, 3.3358)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.8637
Odds Ratio (OR) (95% CI)		1.1295 (0.3537, 3.6062)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.8372
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

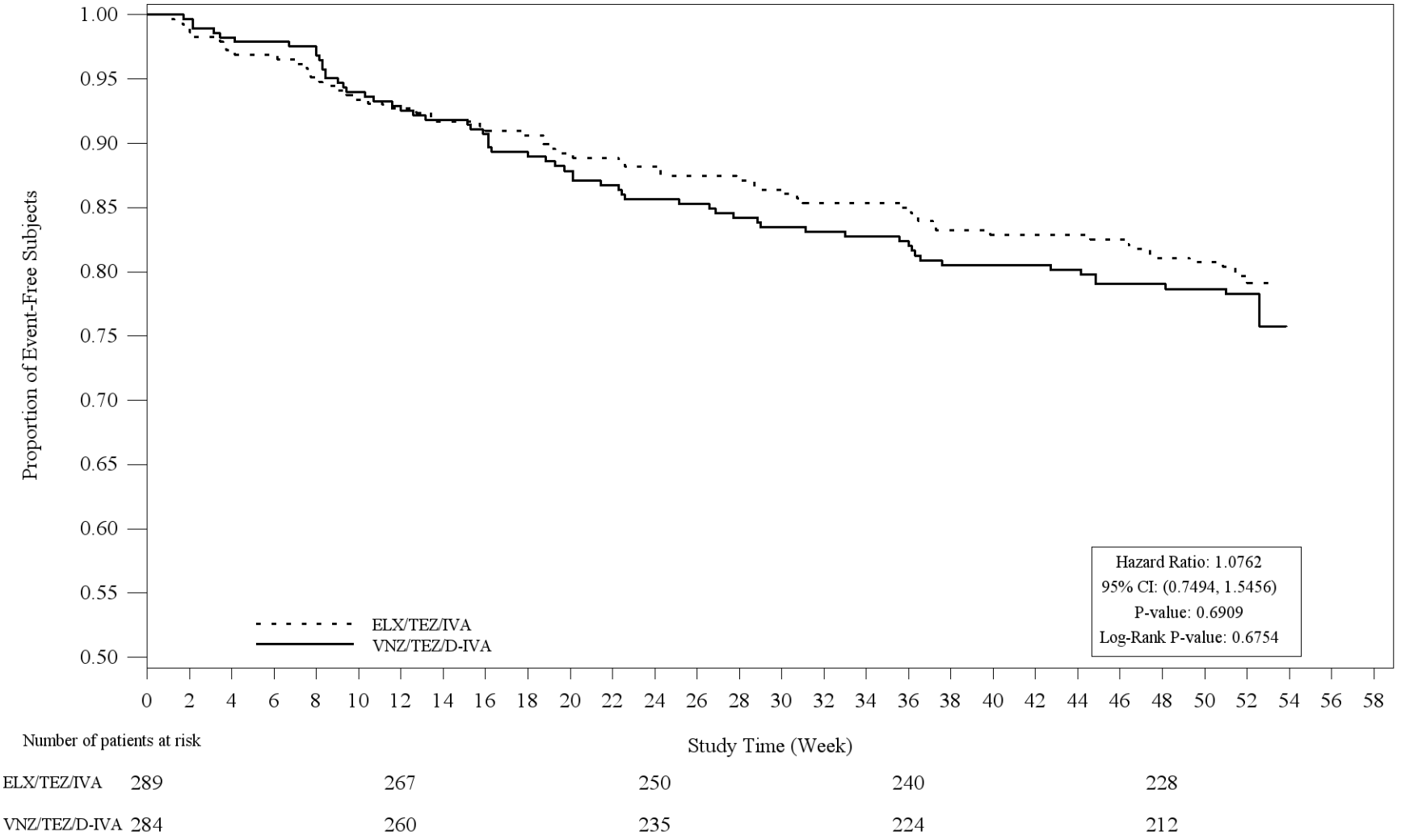
Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	13 (6.99)	9 (5.29)
Relative Risk (RR) (95% CI)		0.8131 (0.3520, 1.8781)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6281
Odds Ratio (OR) (95% CI)		0.8166 (0.3317, 2.0103)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6593
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Figure 2.2.1.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52
Full Analysis Set

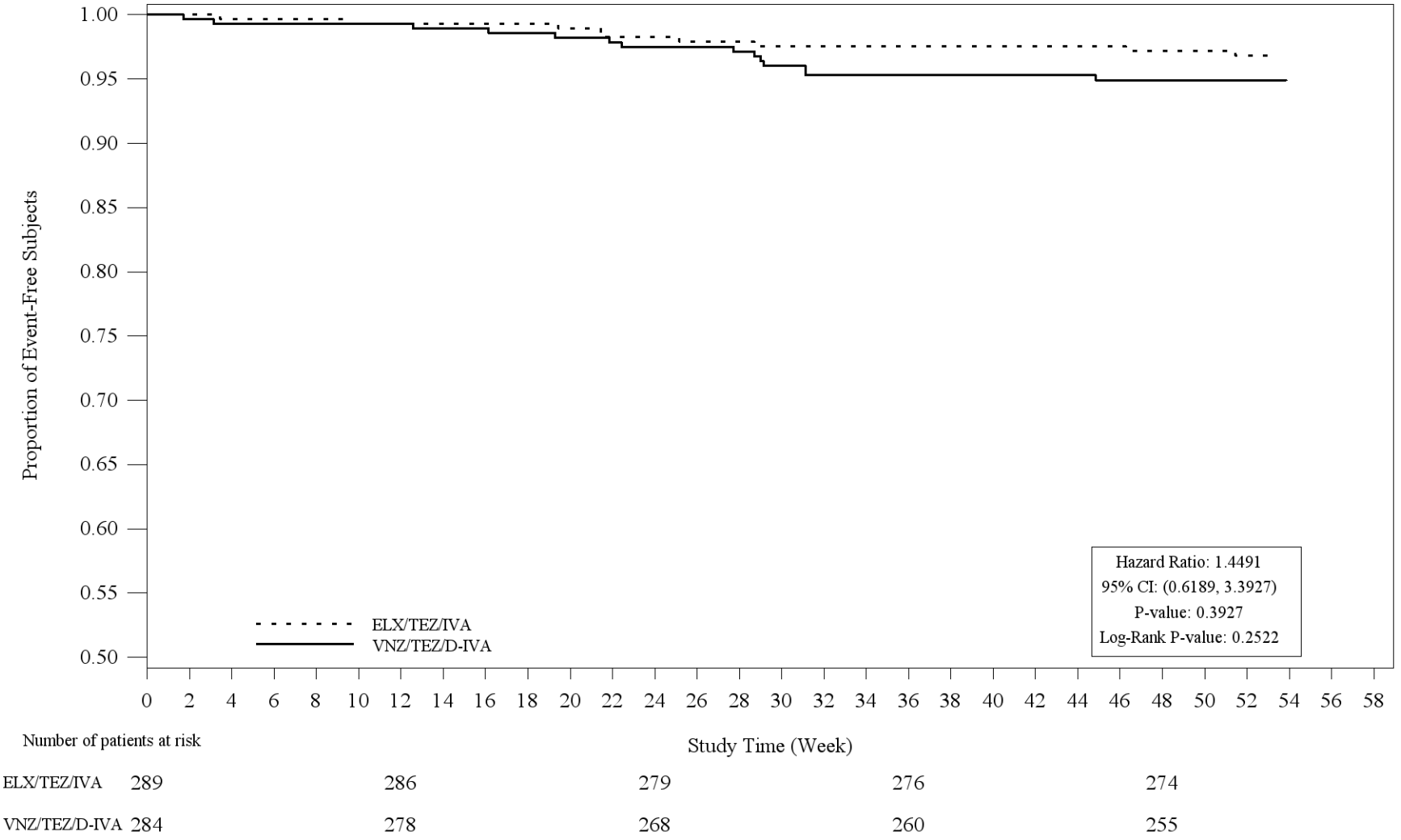


Number of patients at risk

ELX/TEZ/IVA	289	267	250	240	228
VNZ/TEZ/D-IVA	284	260	235	224	212

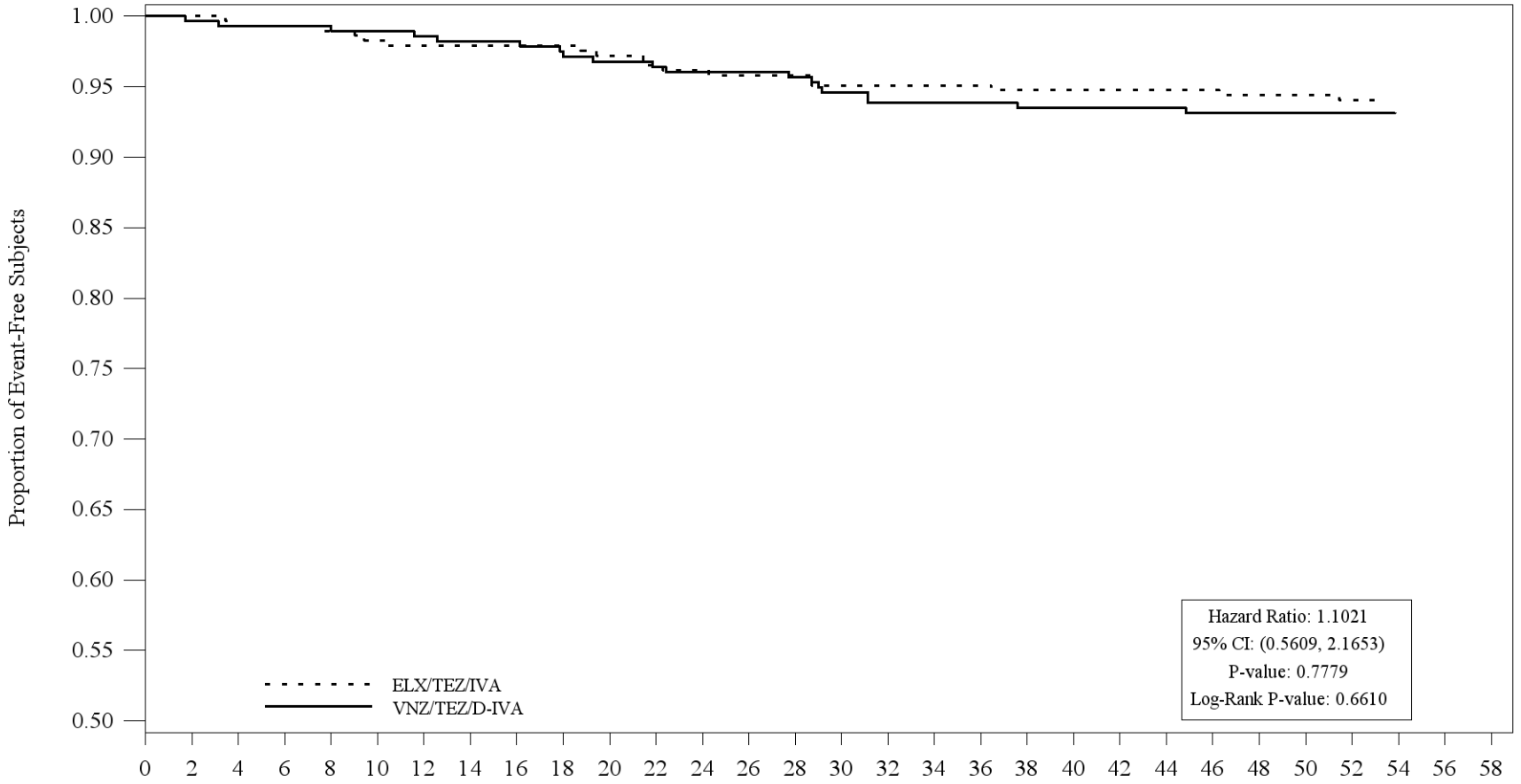
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 2.2.1.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set



- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 2.2.1.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set



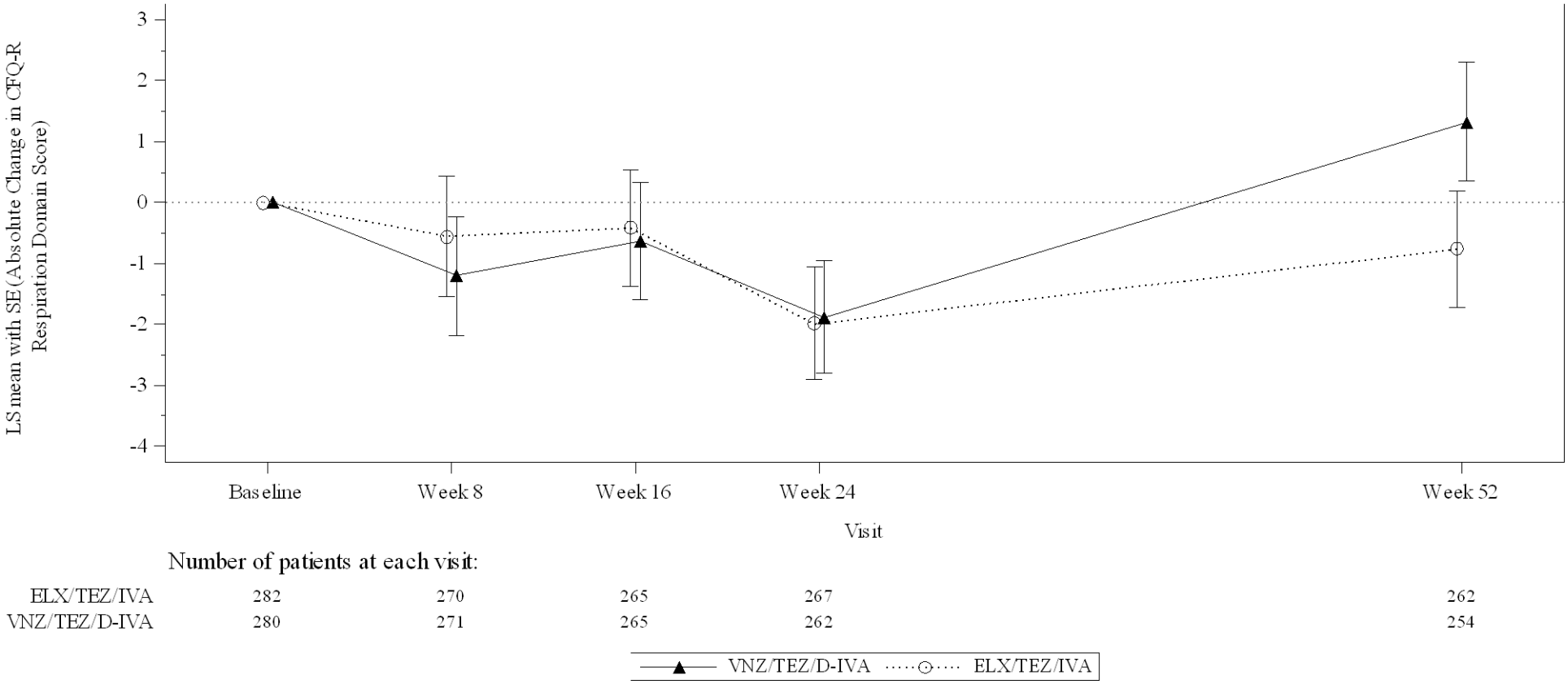
Number of patients at risk

ELX/TEZ/IVA	289	282	273	269	266
VNZ/TEZ/D-IVA	284	276	264	256	250

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

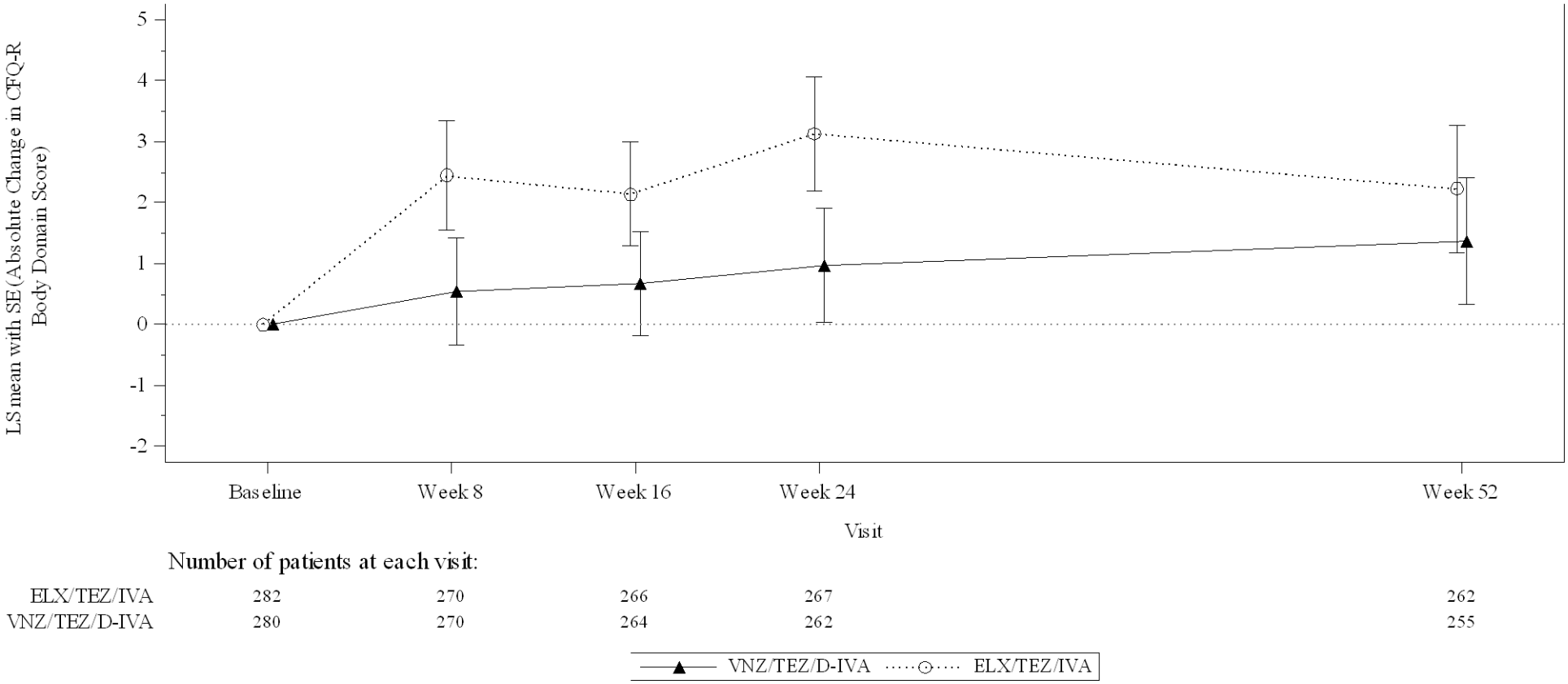
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

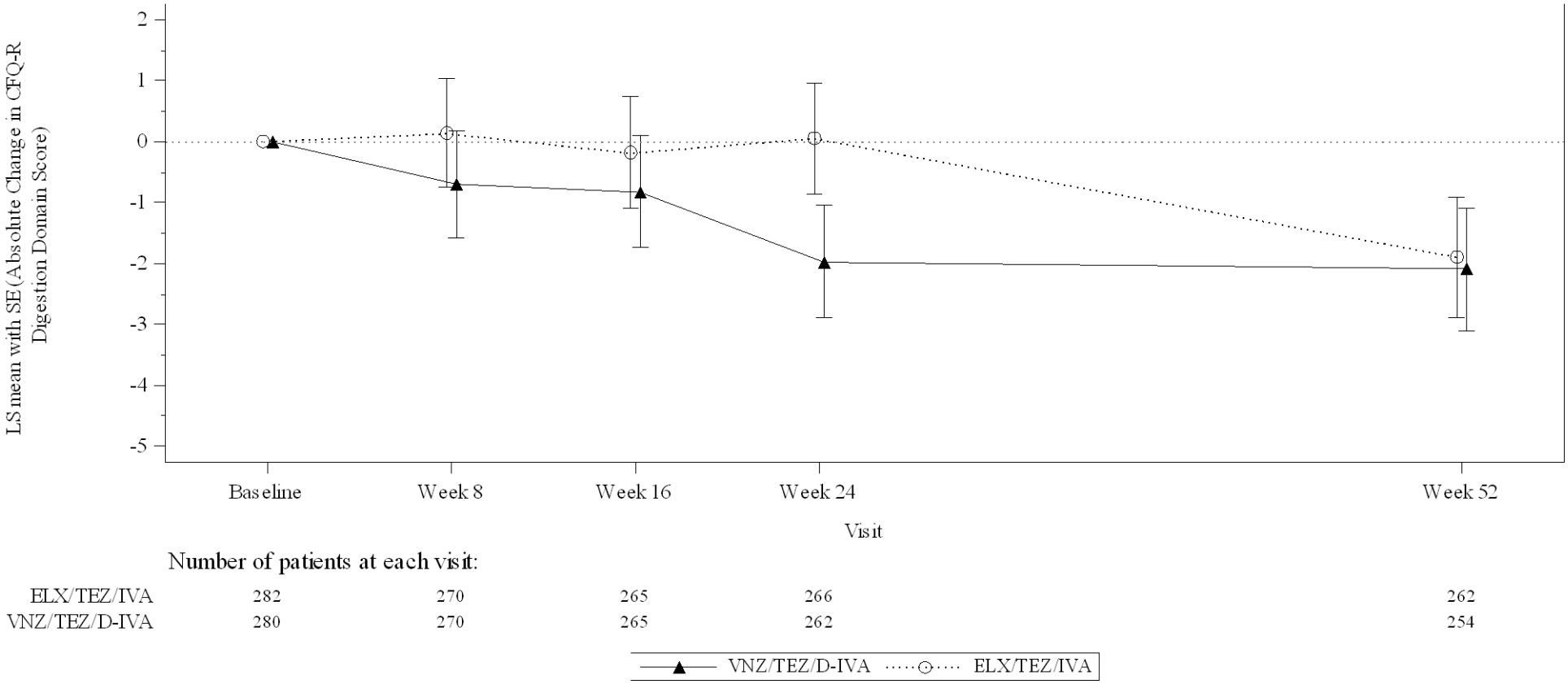


- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

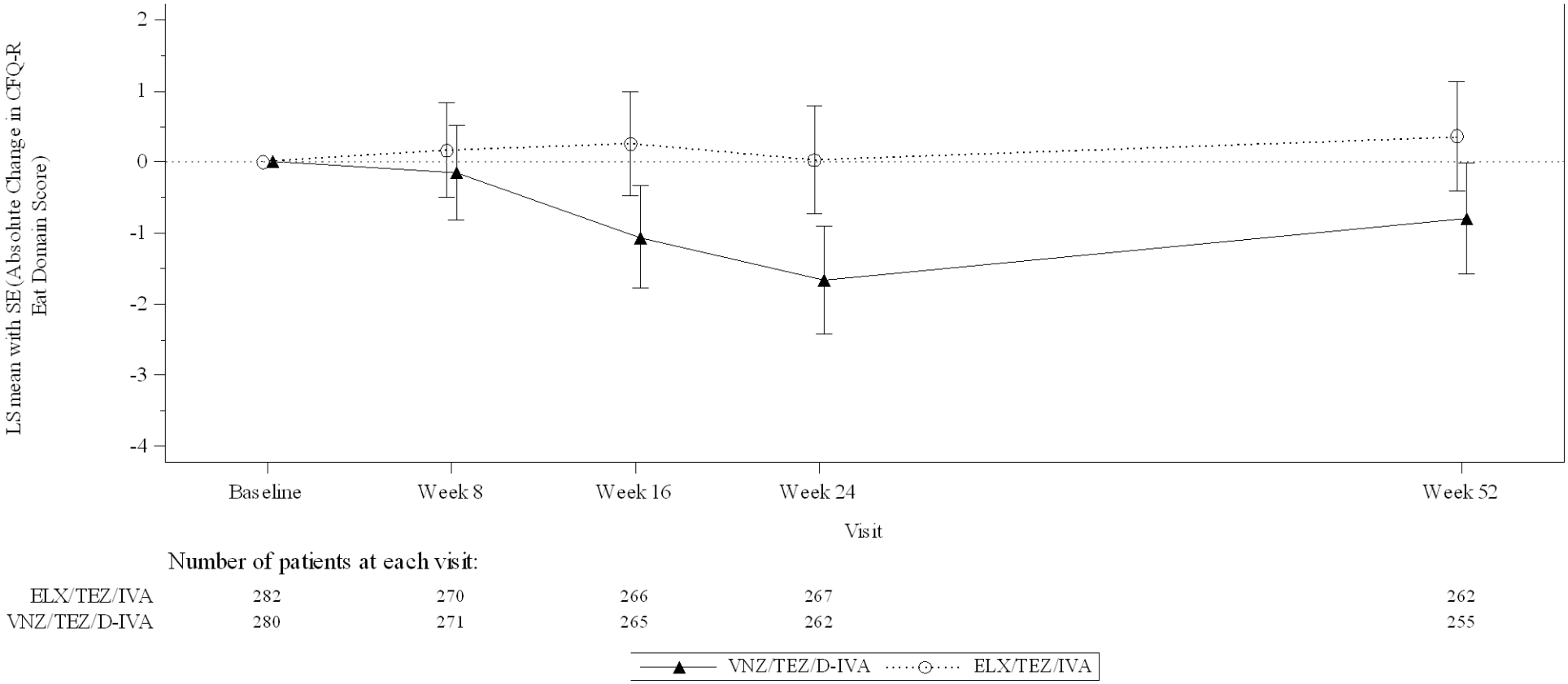


- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

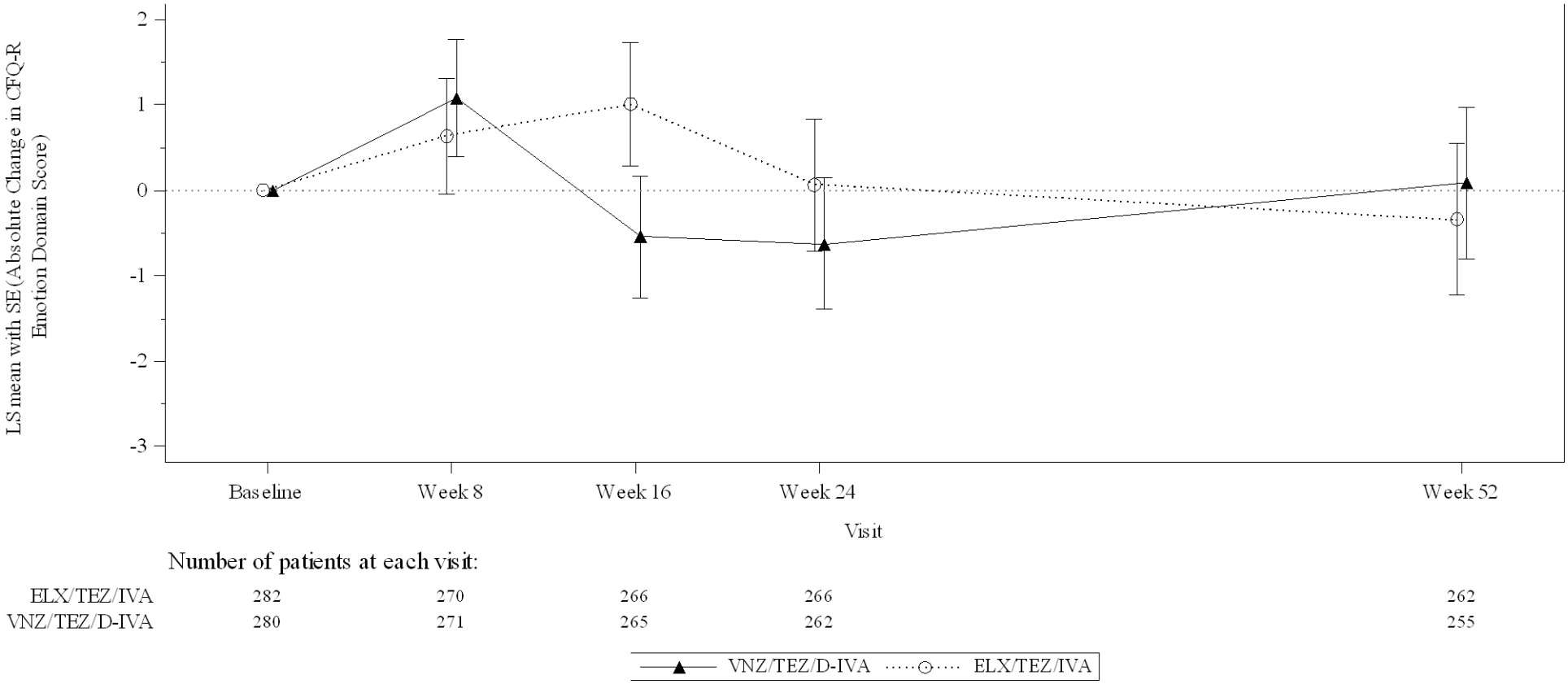


- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

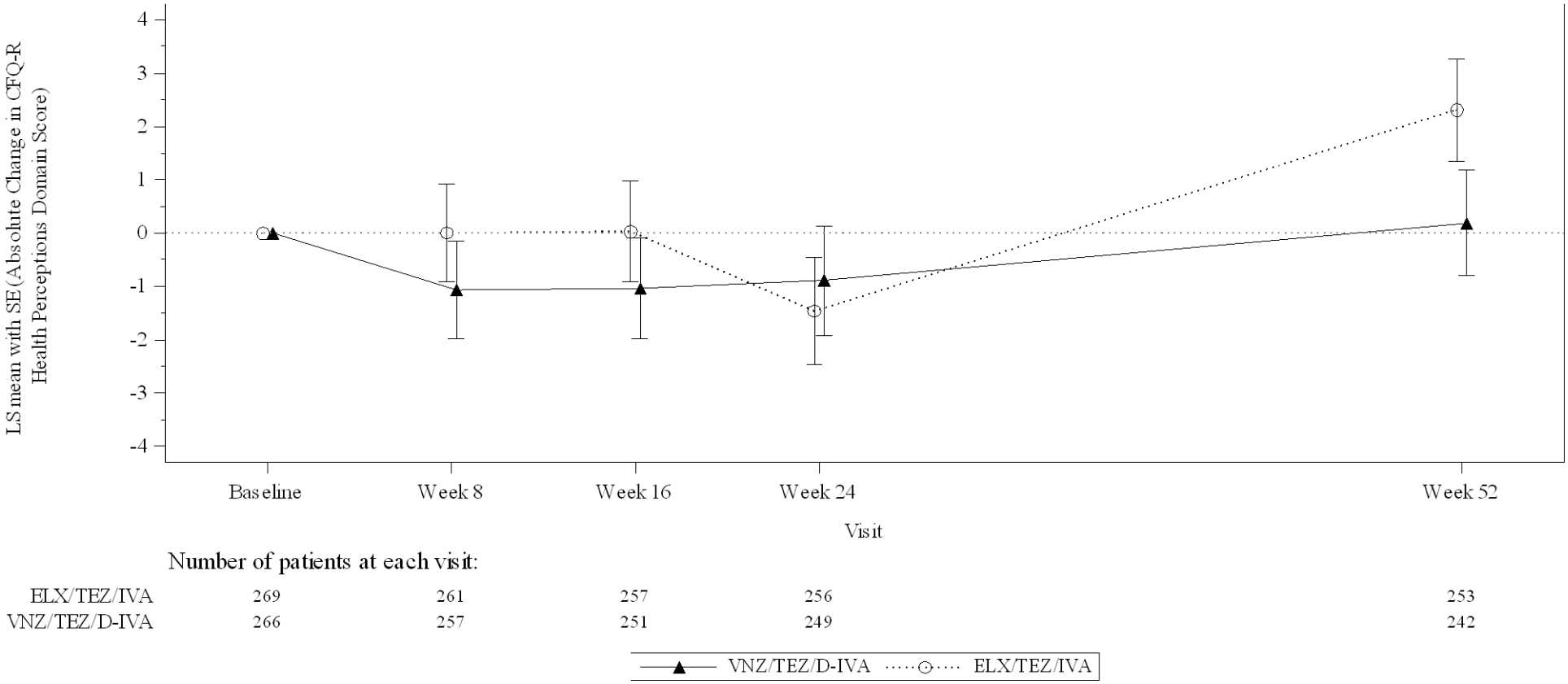


- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions

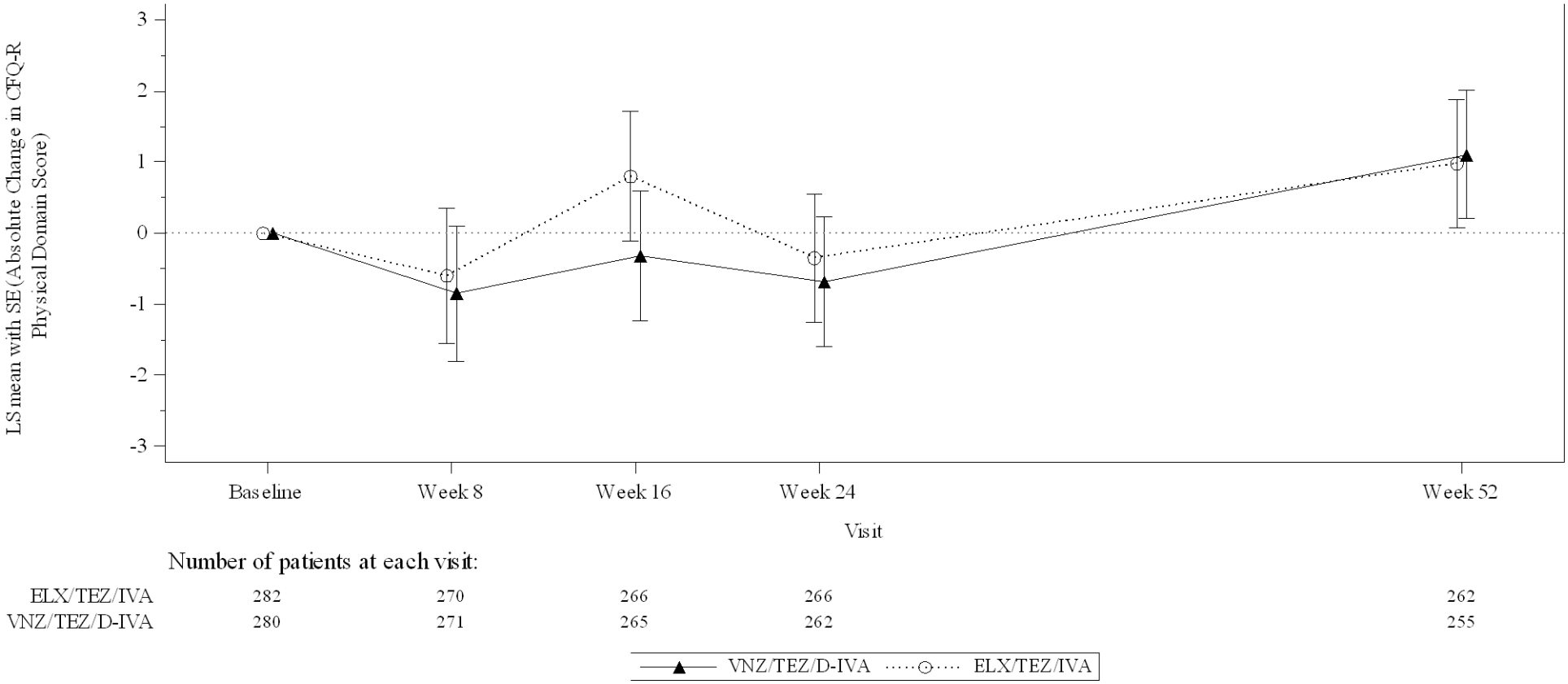


- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

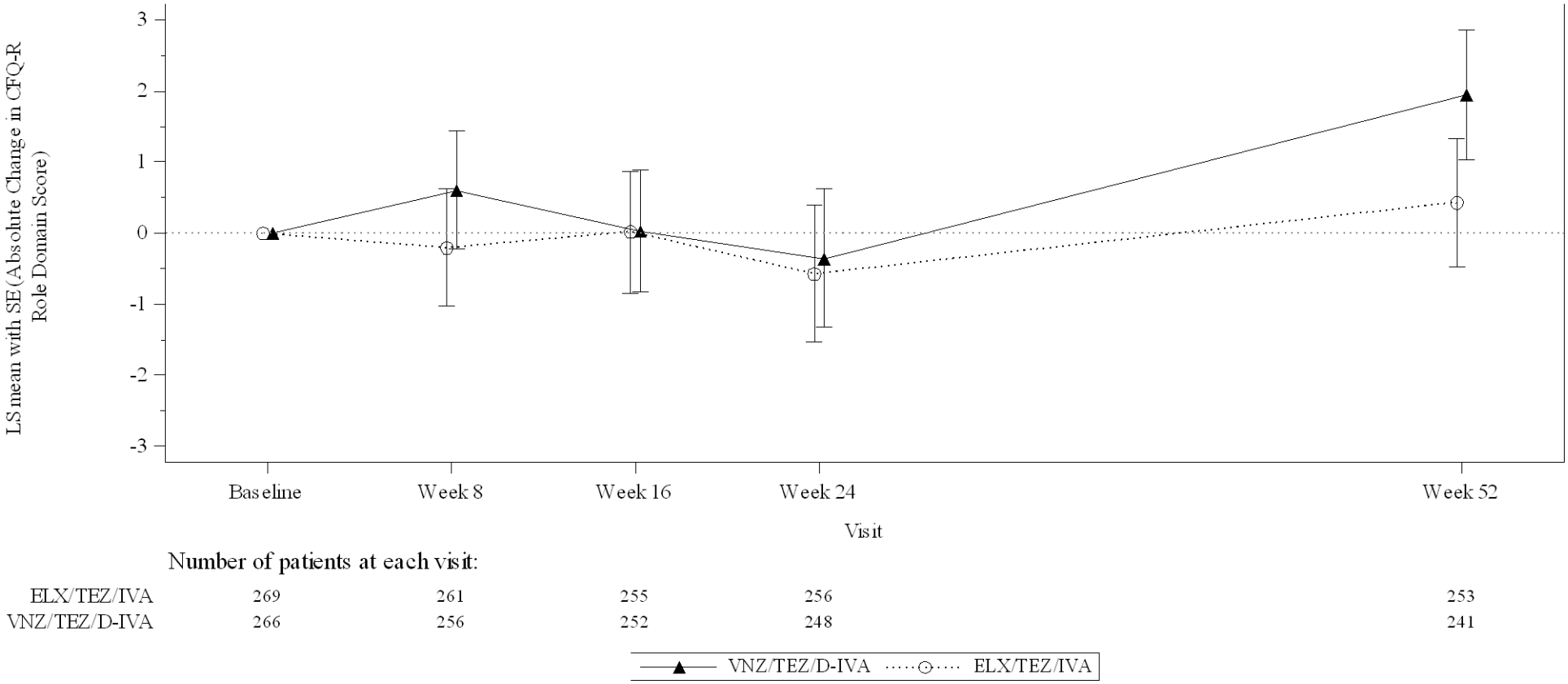


- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role

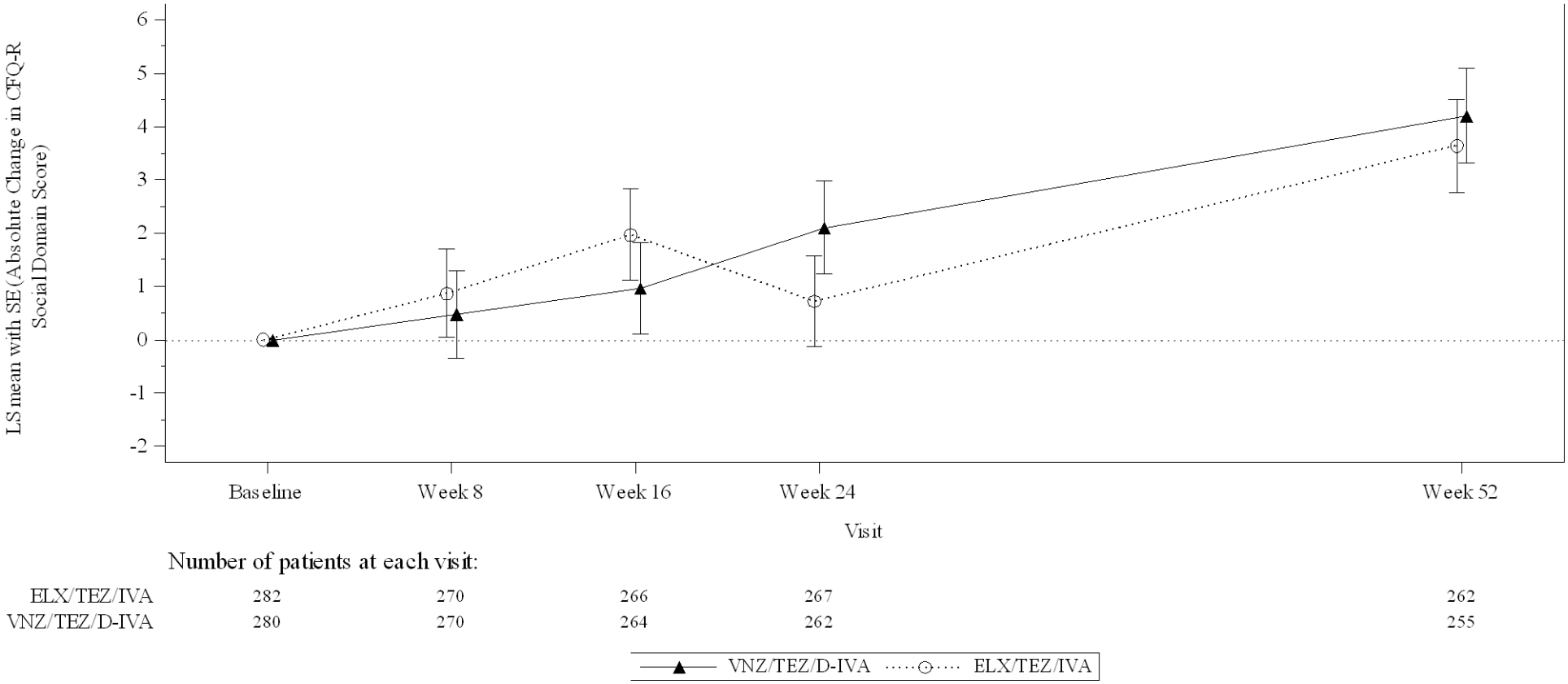


- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

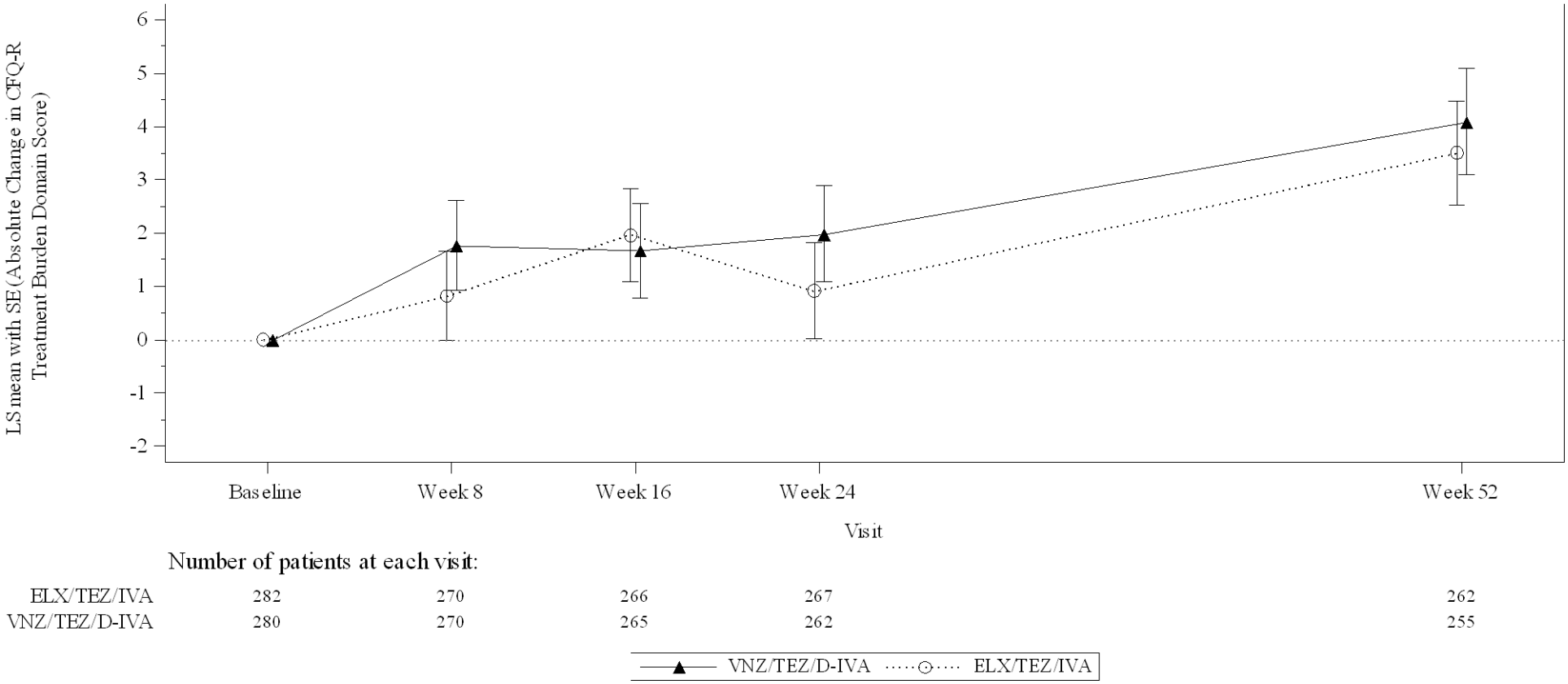


- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

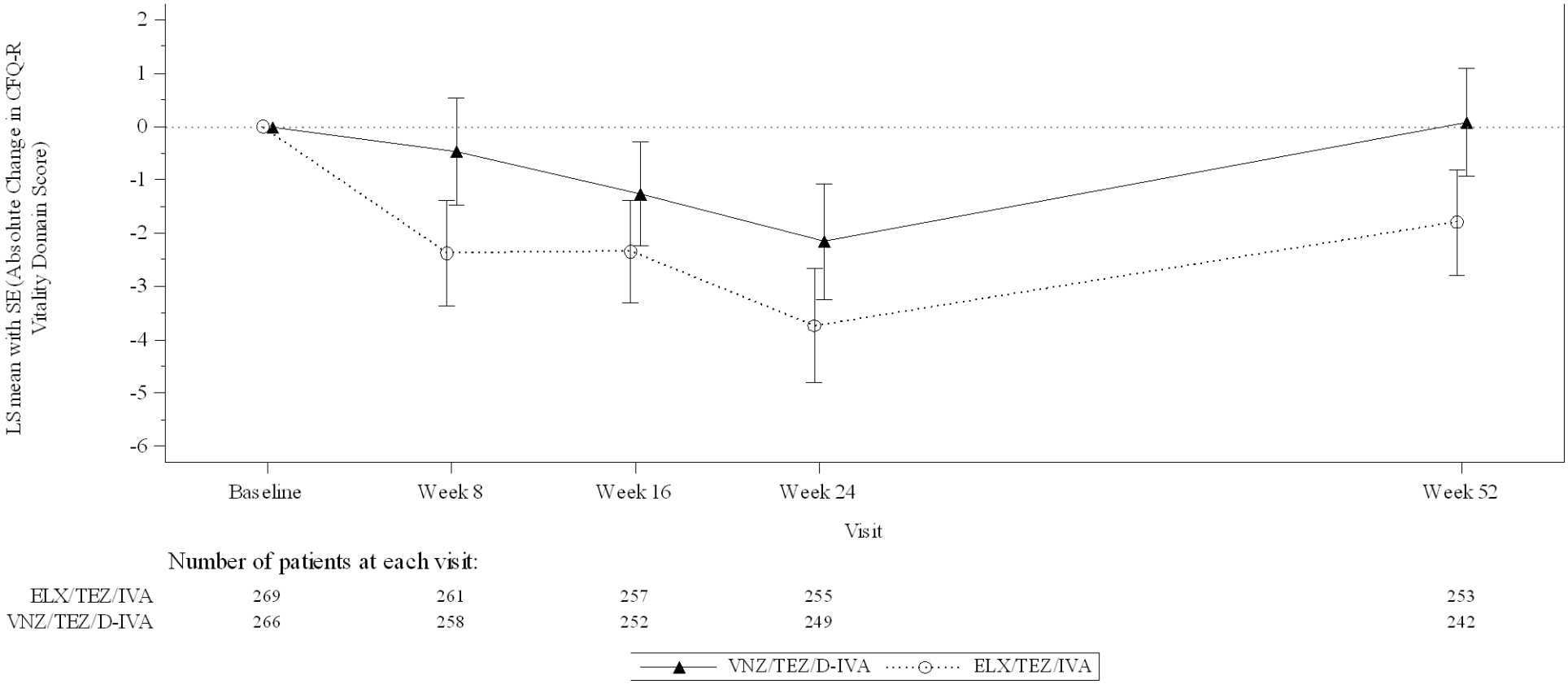


- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality

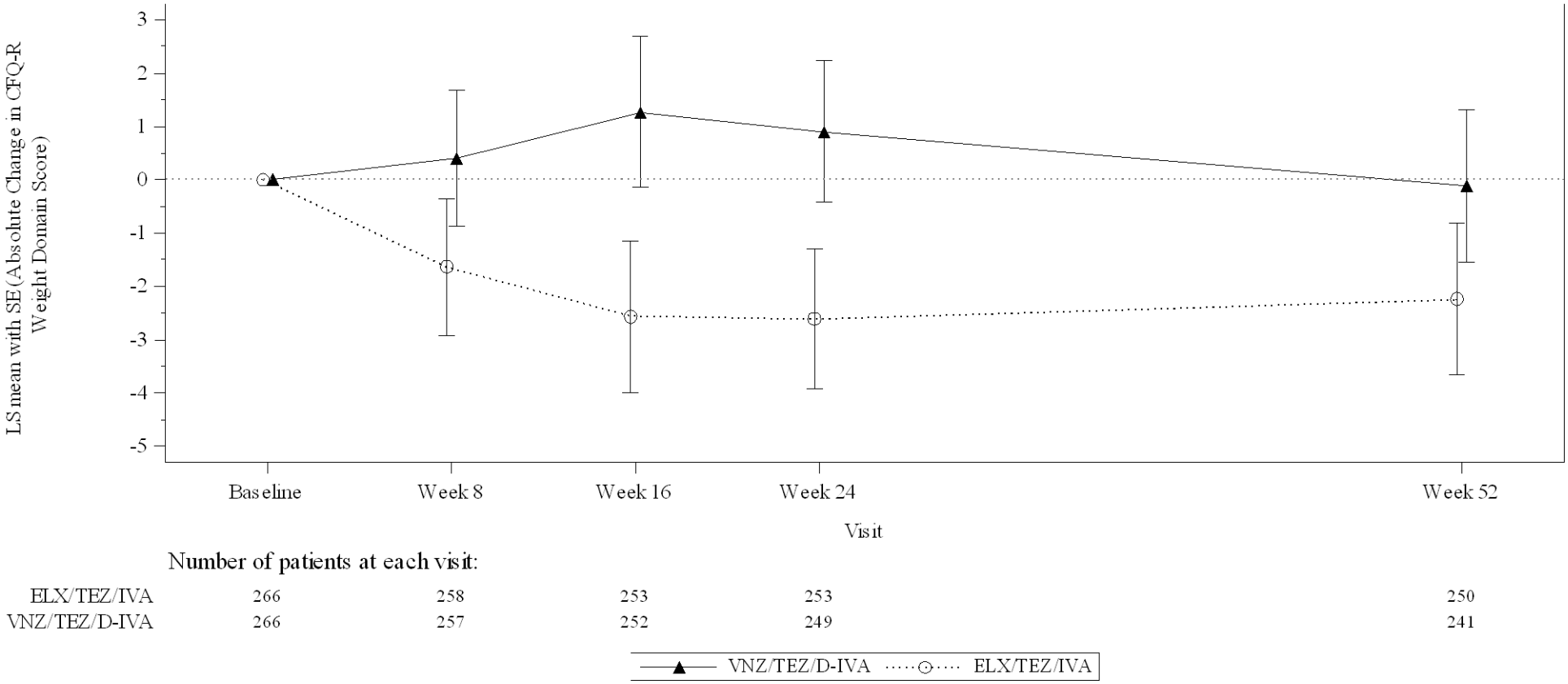


- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight



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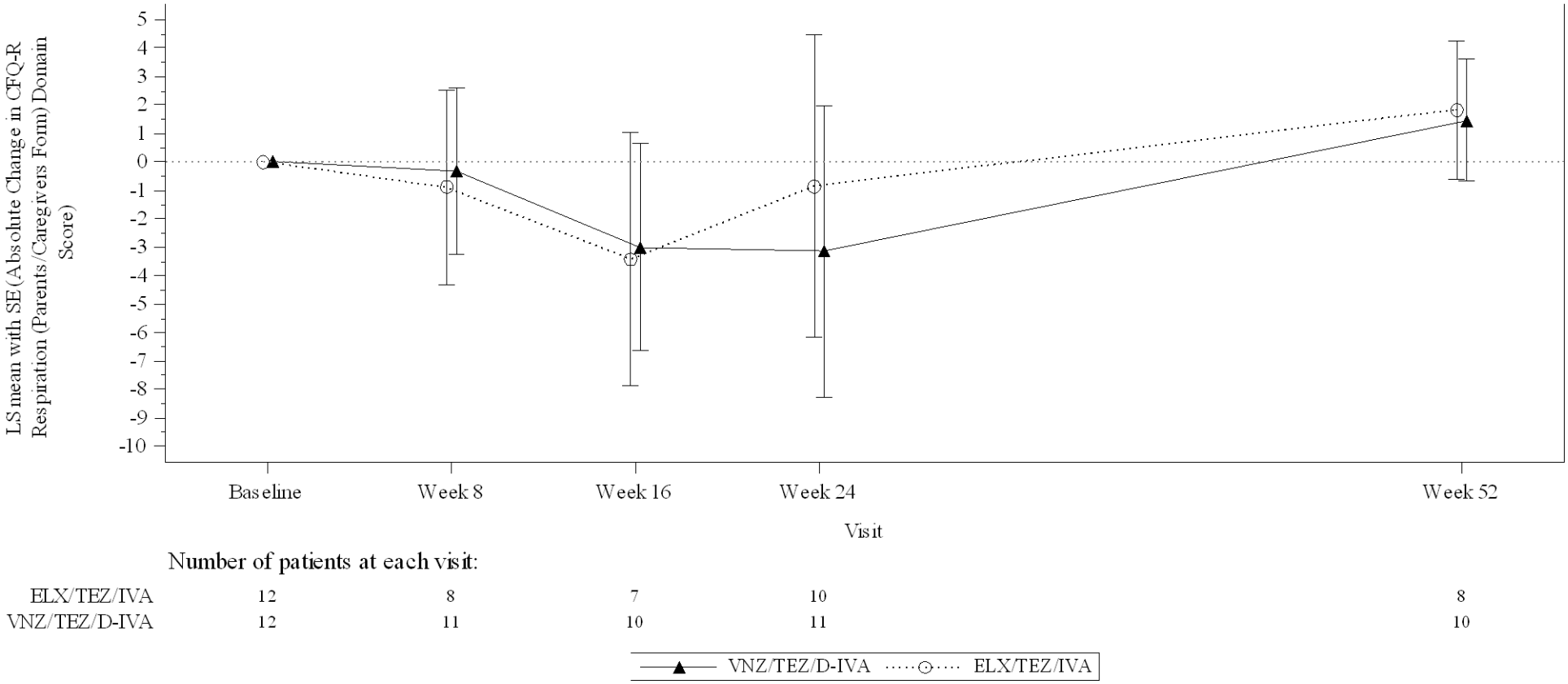
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)



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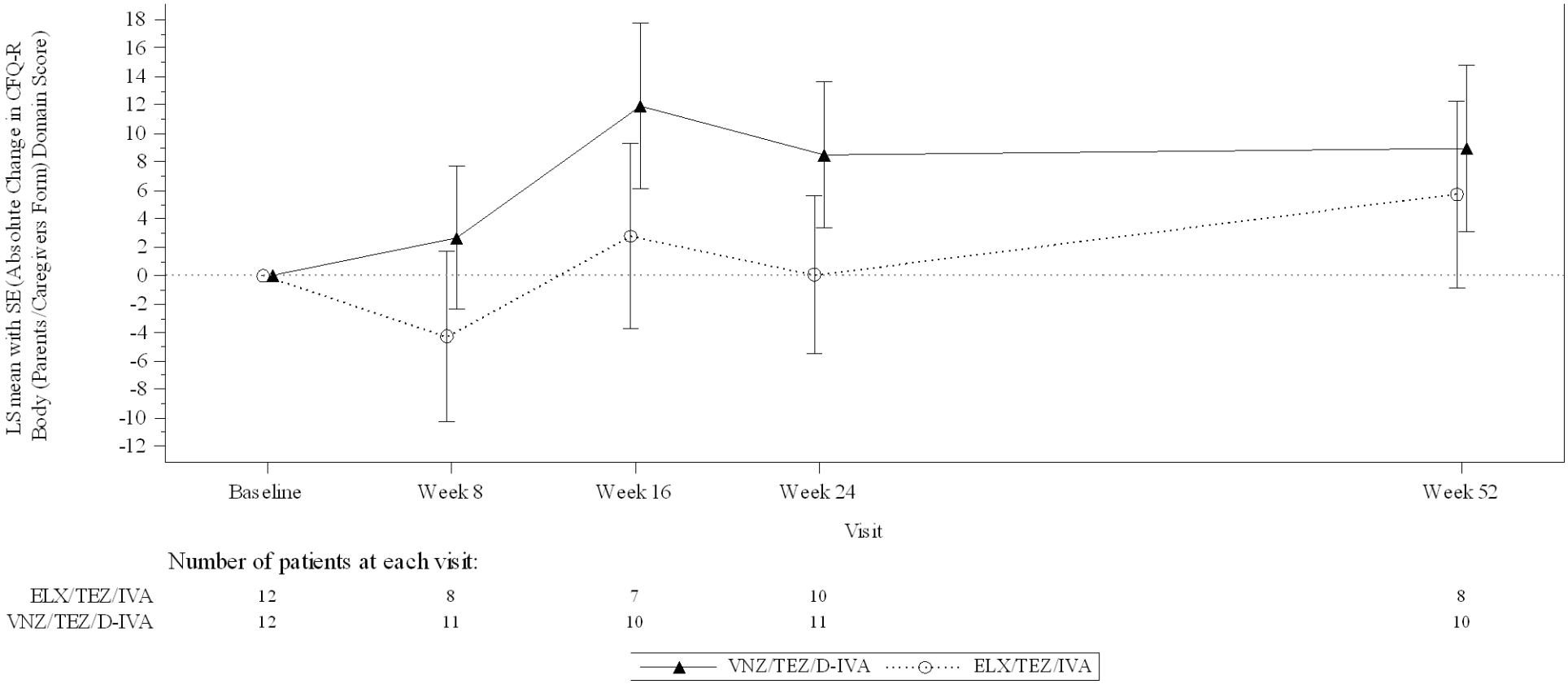
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)



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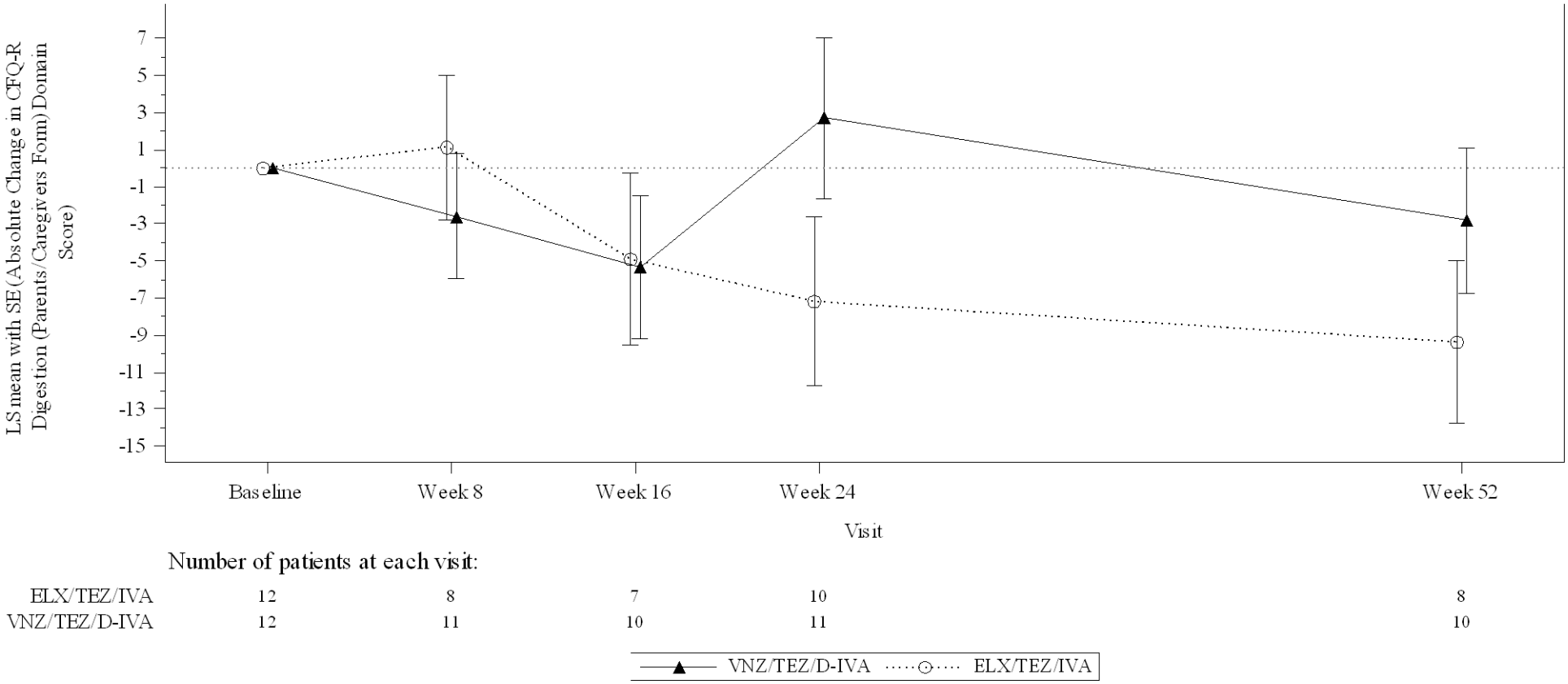
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)



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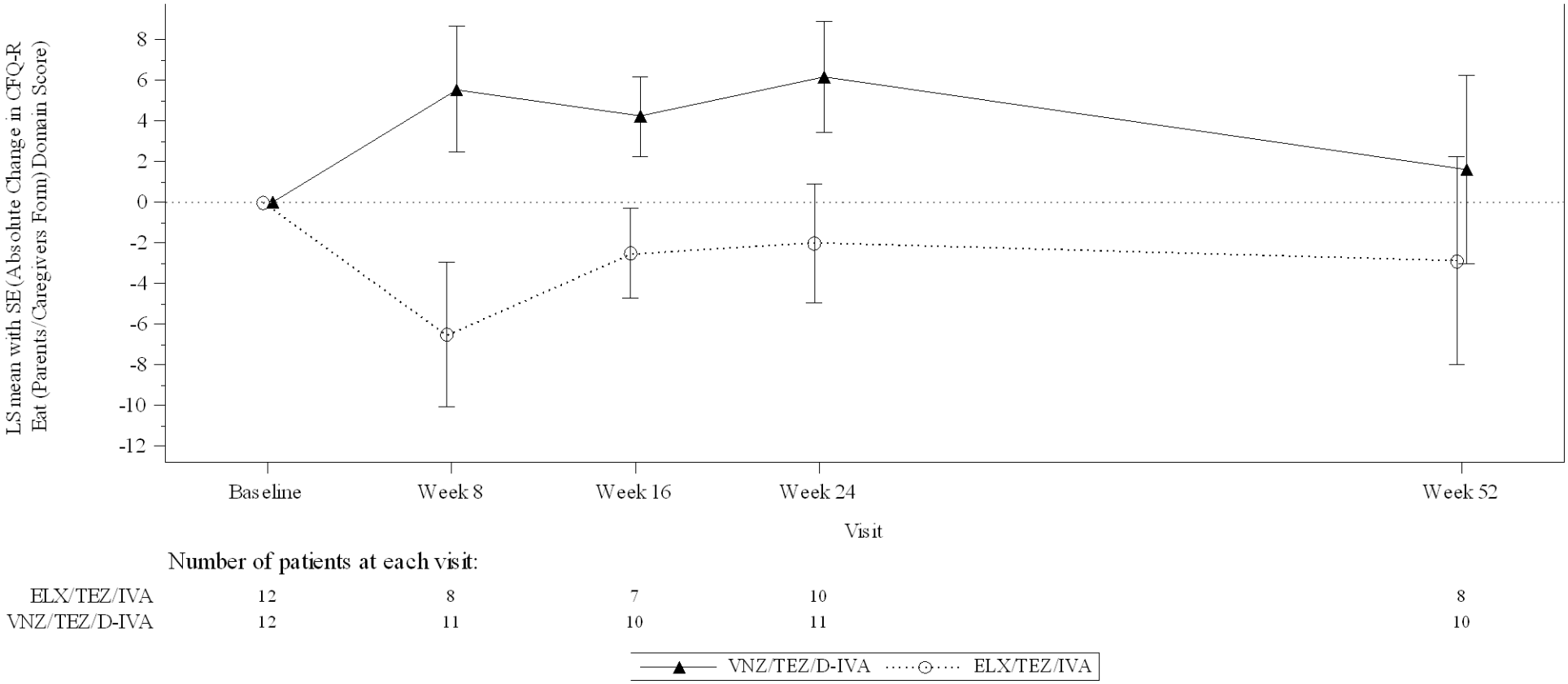
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)



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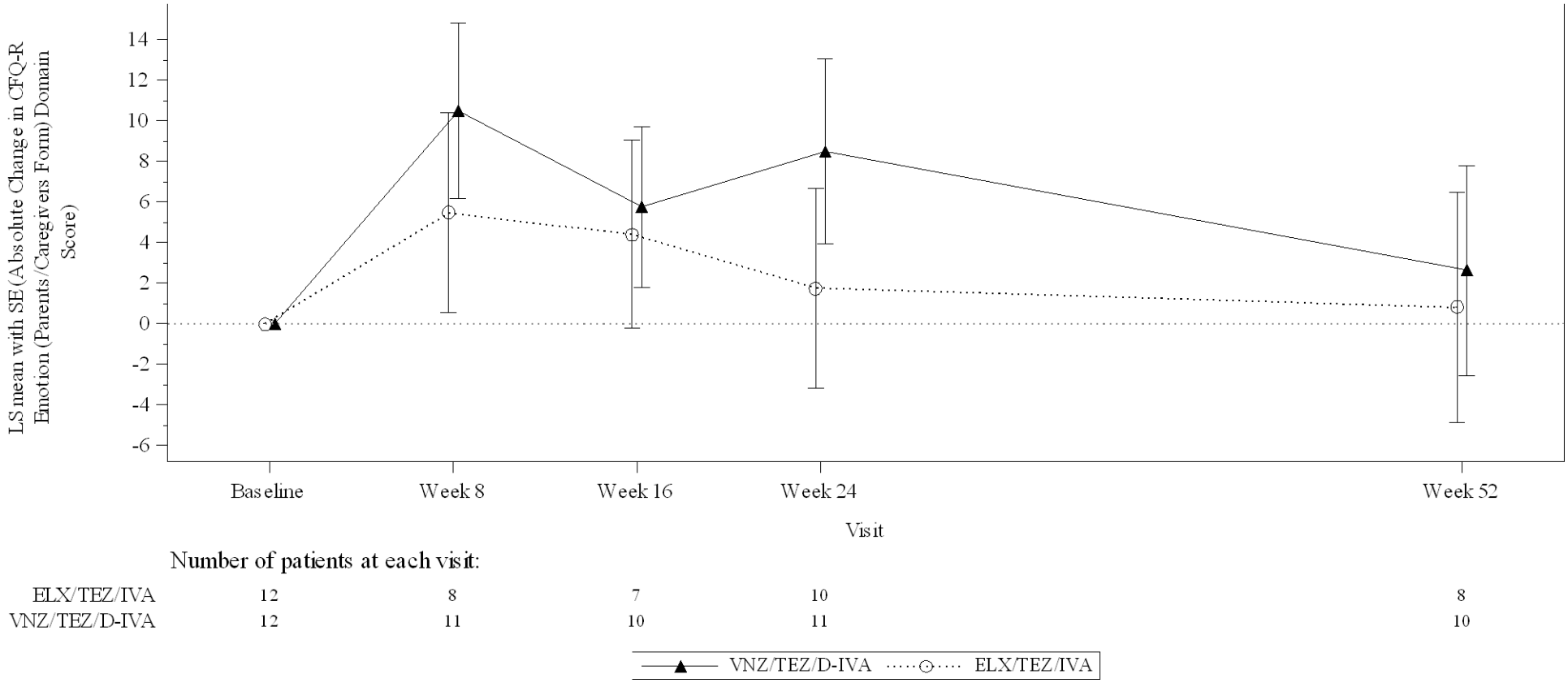
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)



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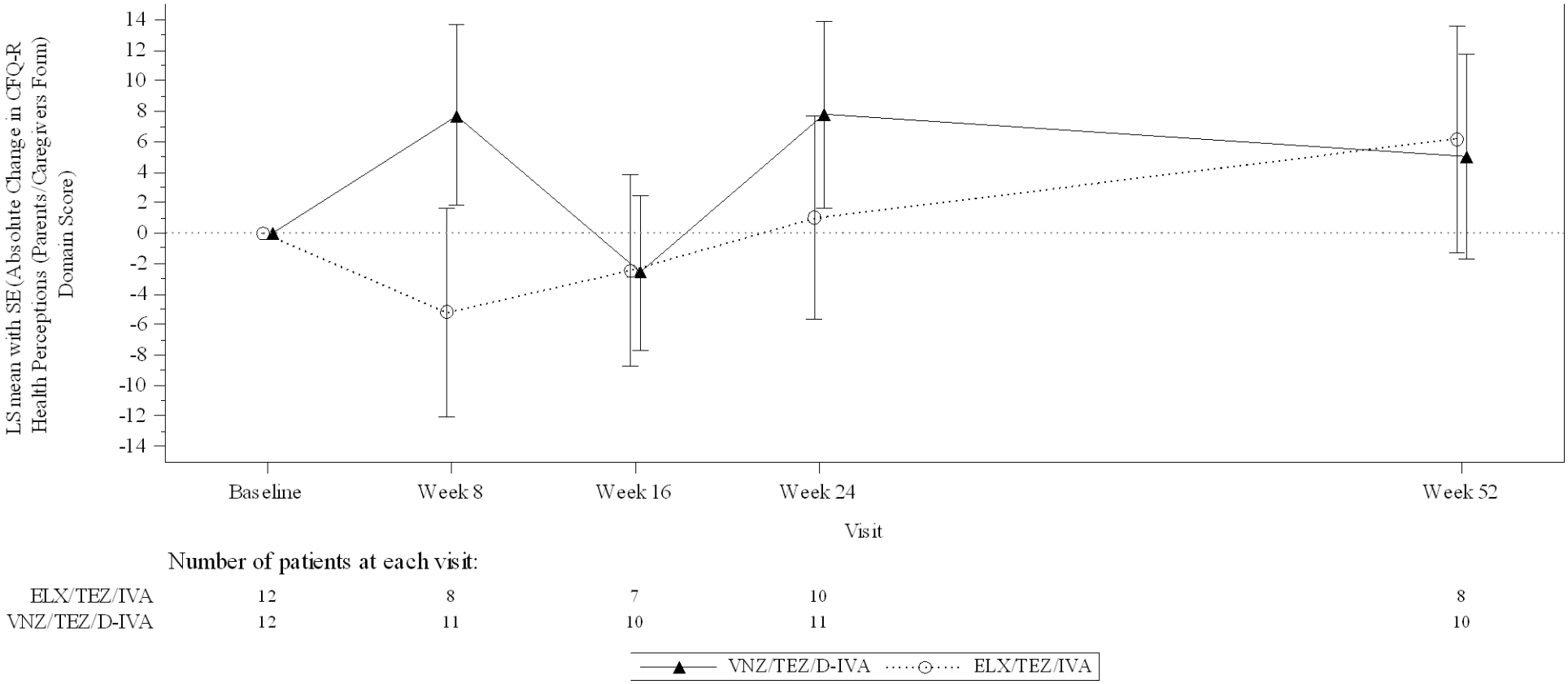
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)



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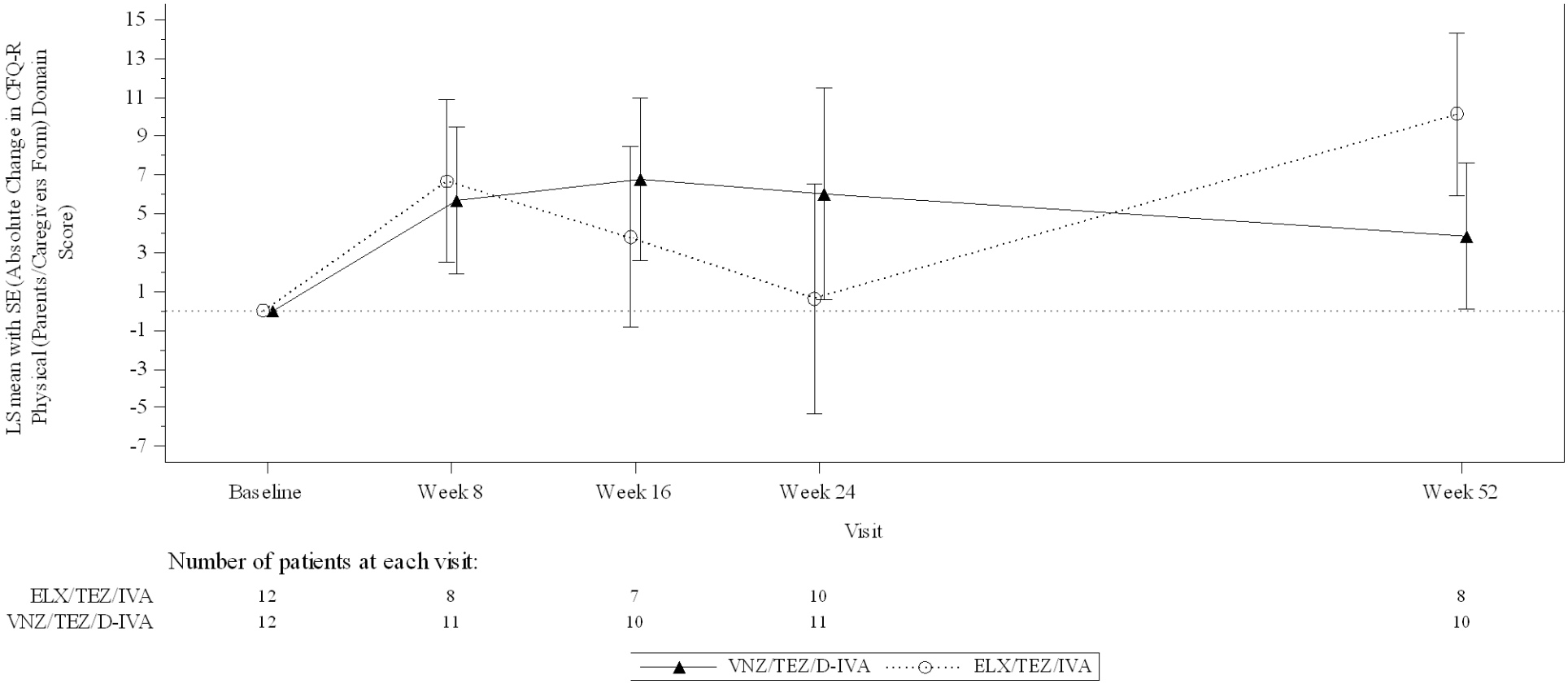
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)



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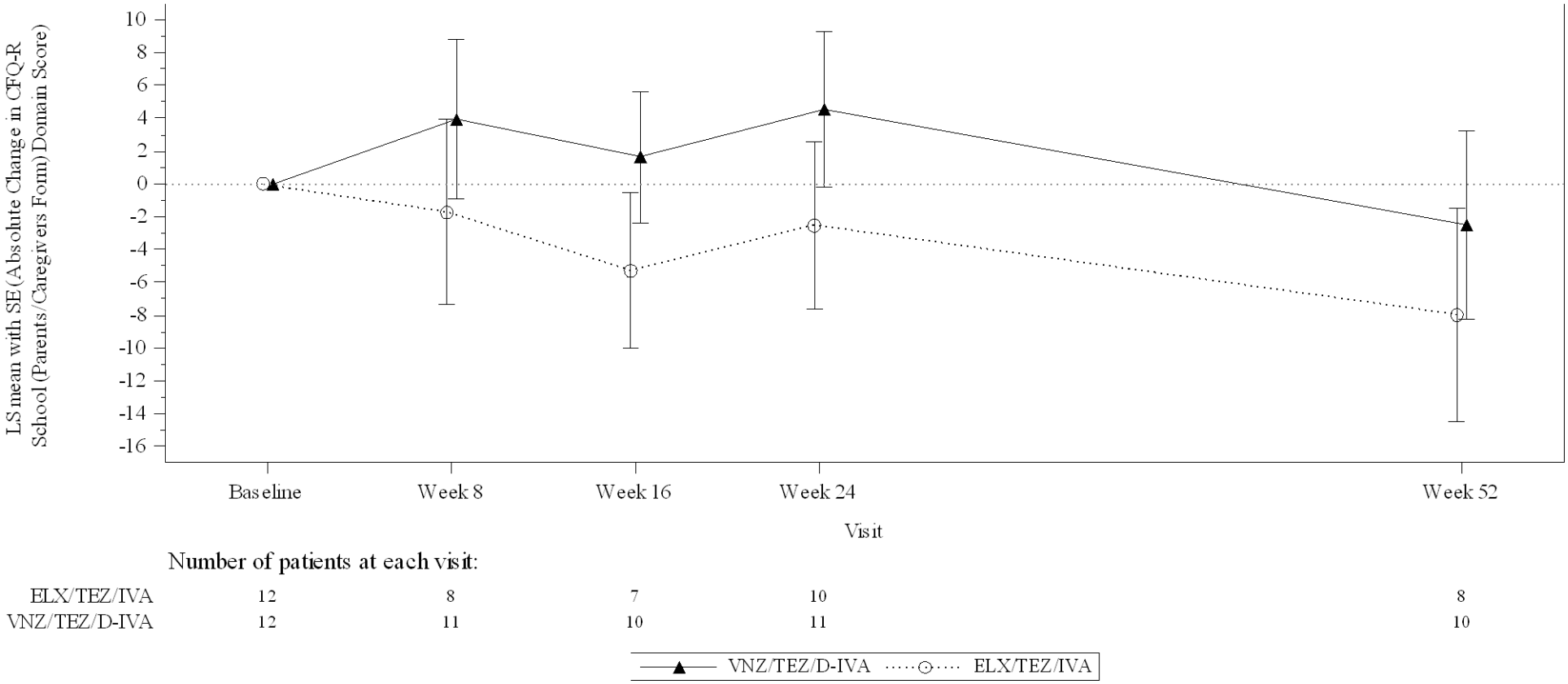
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)



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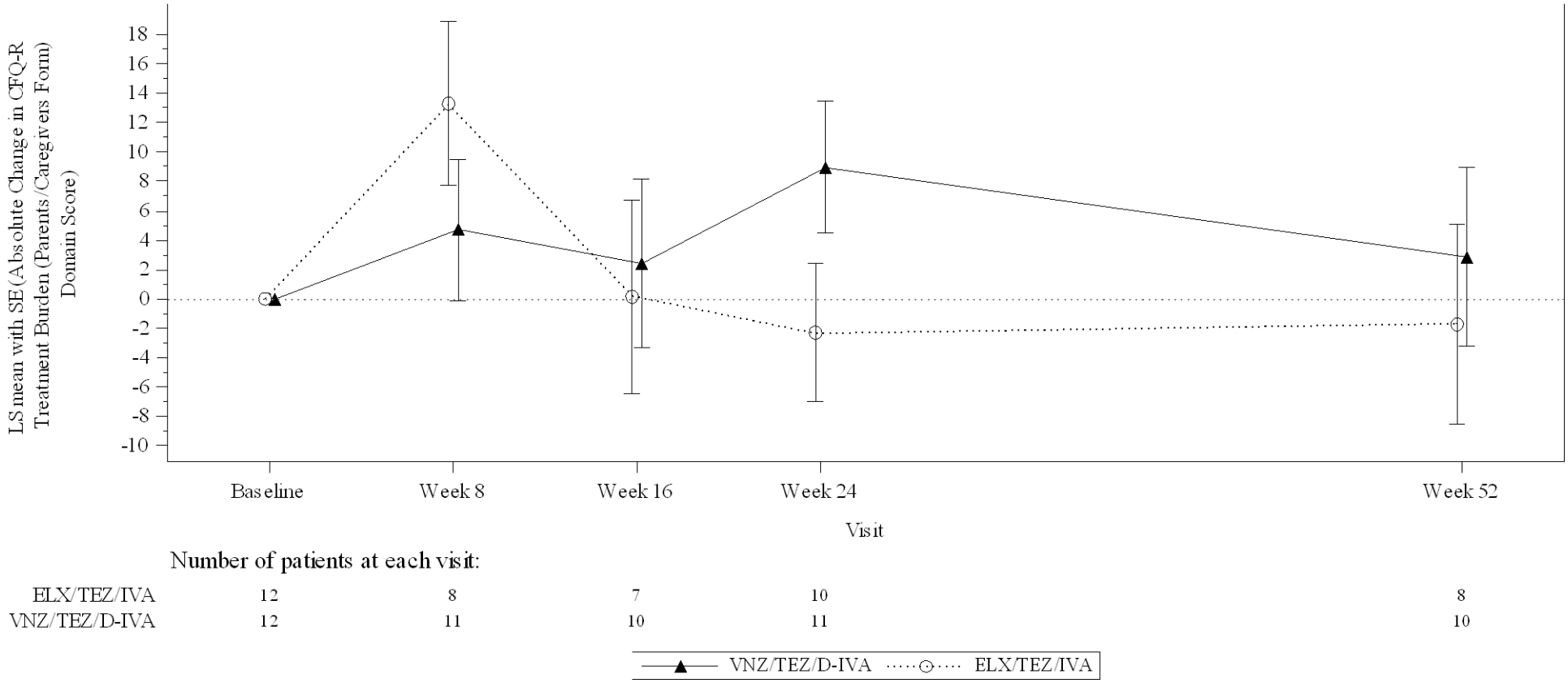
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)



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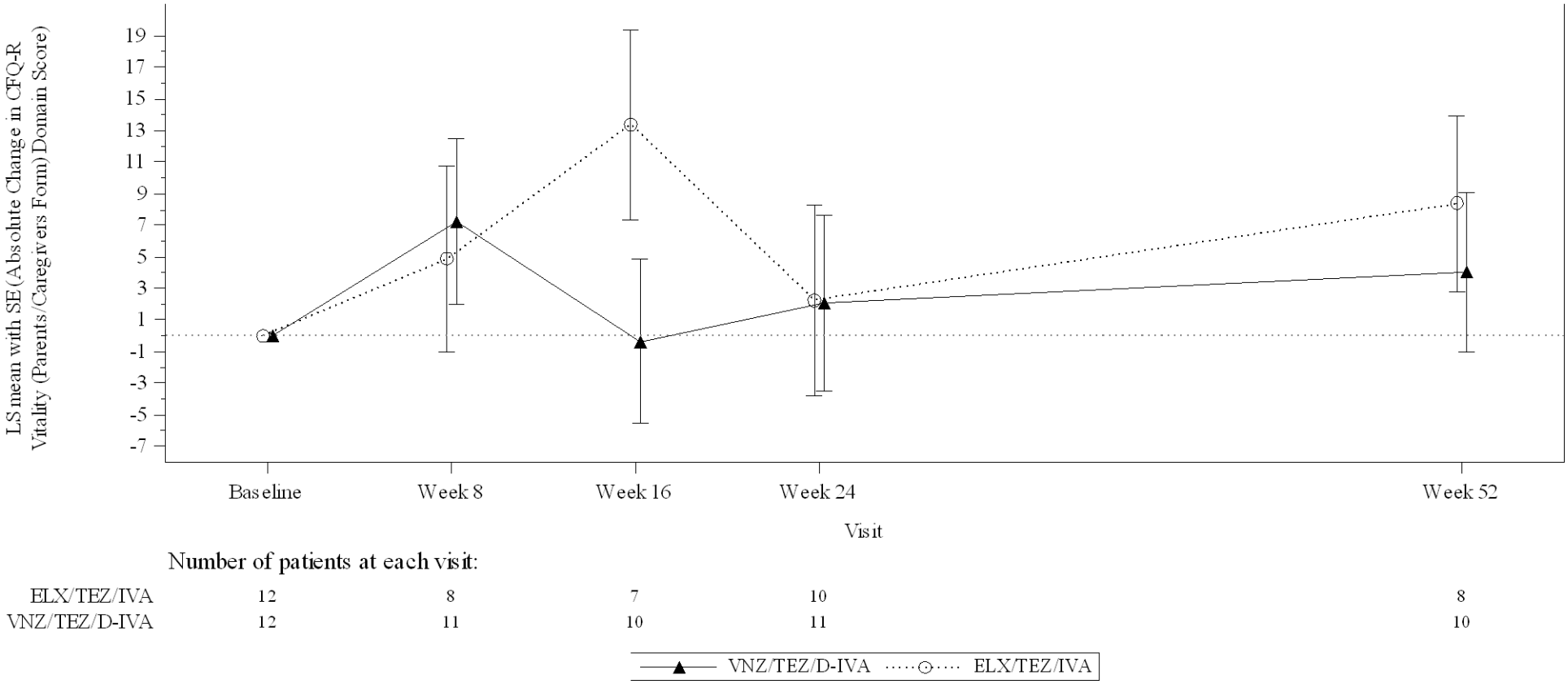
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)



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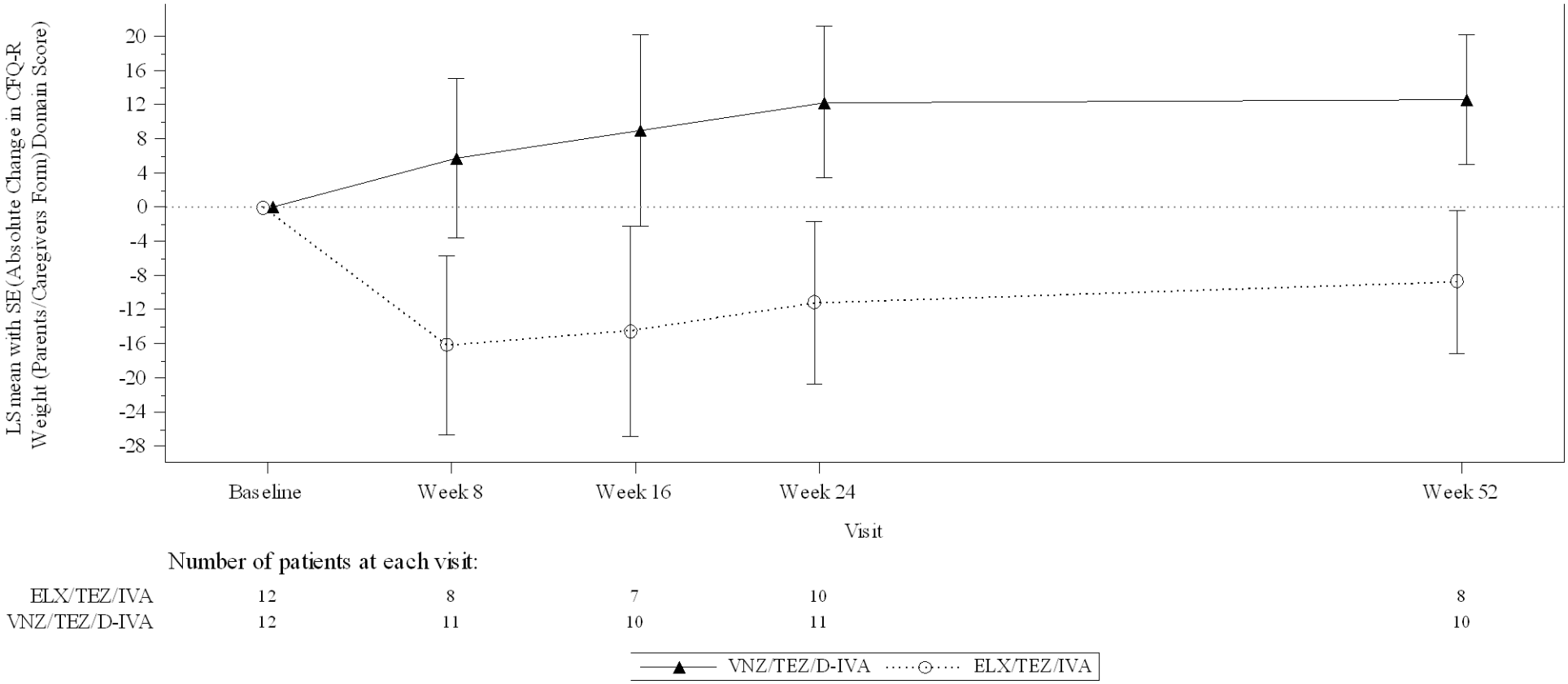
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)



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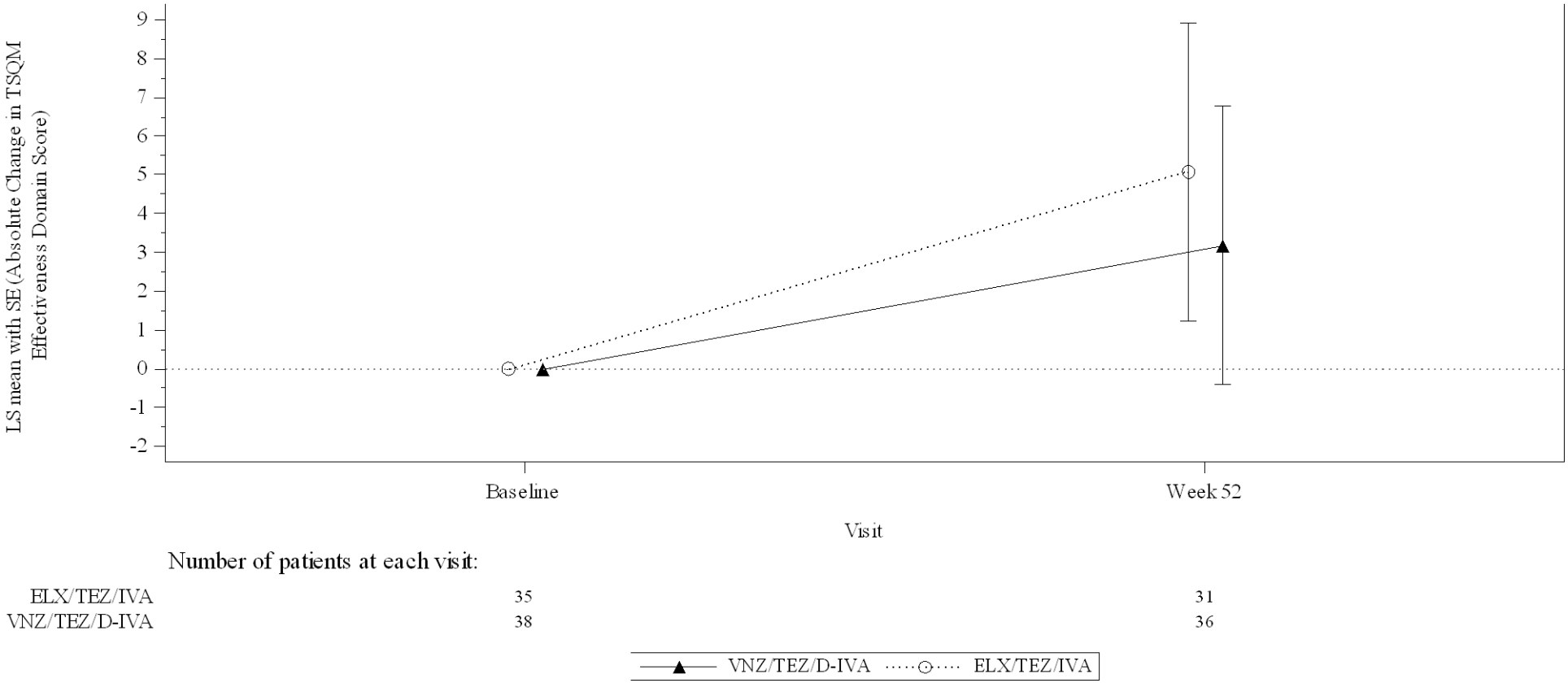
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness



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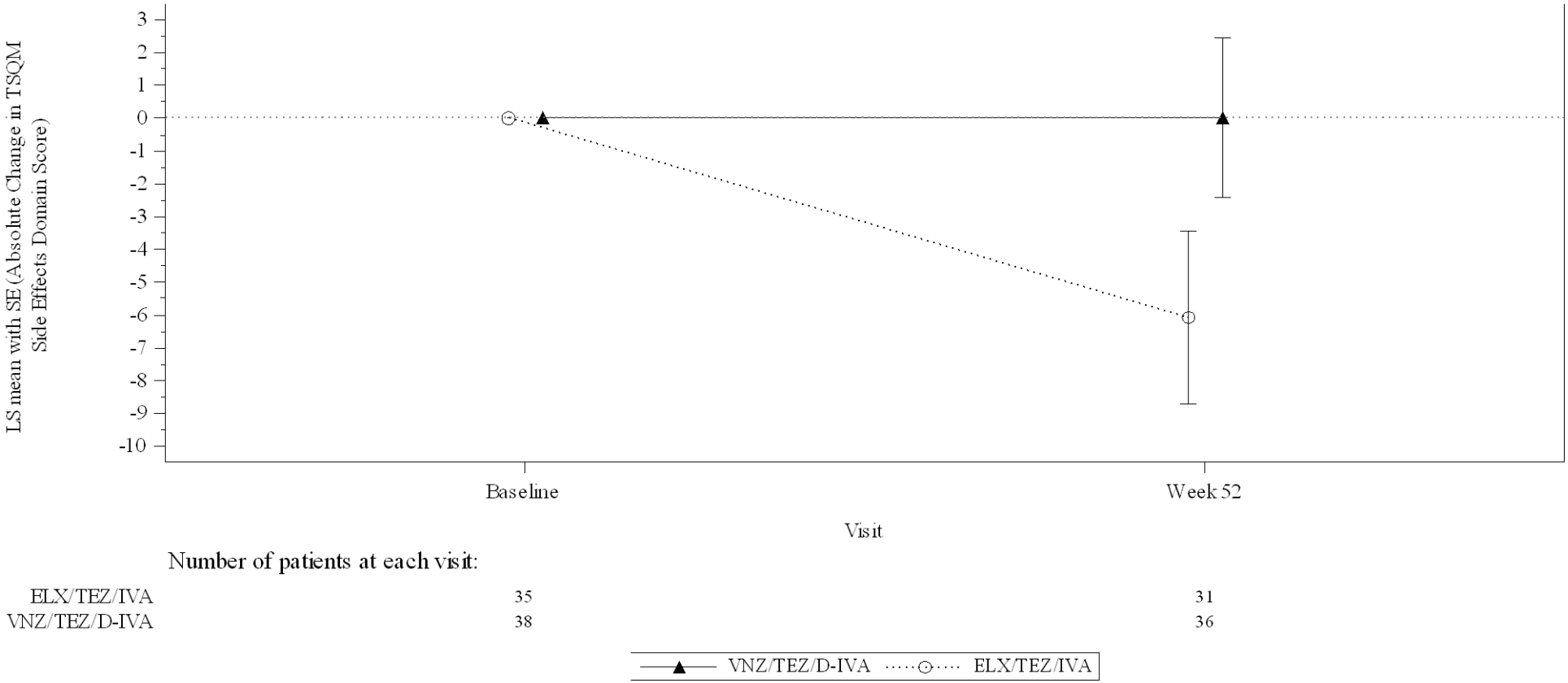
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects



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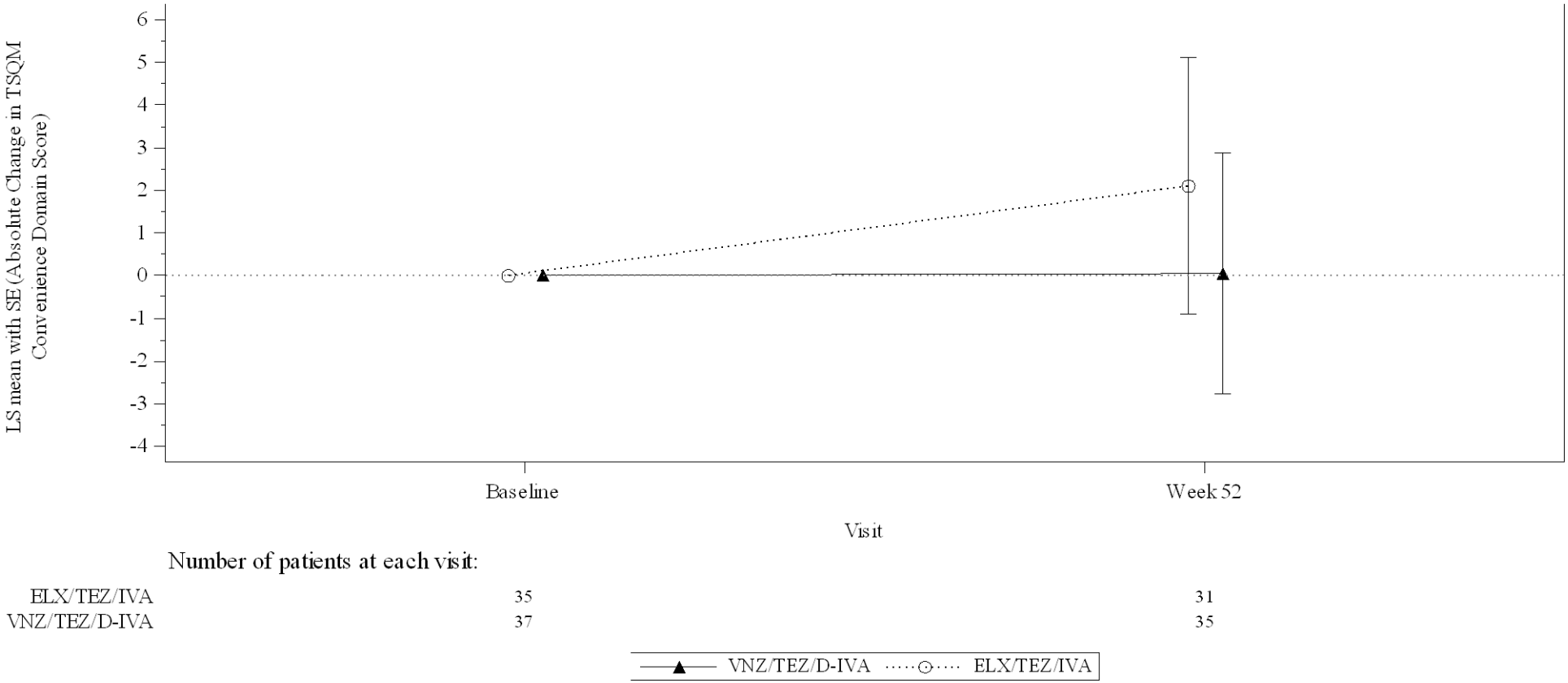
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience



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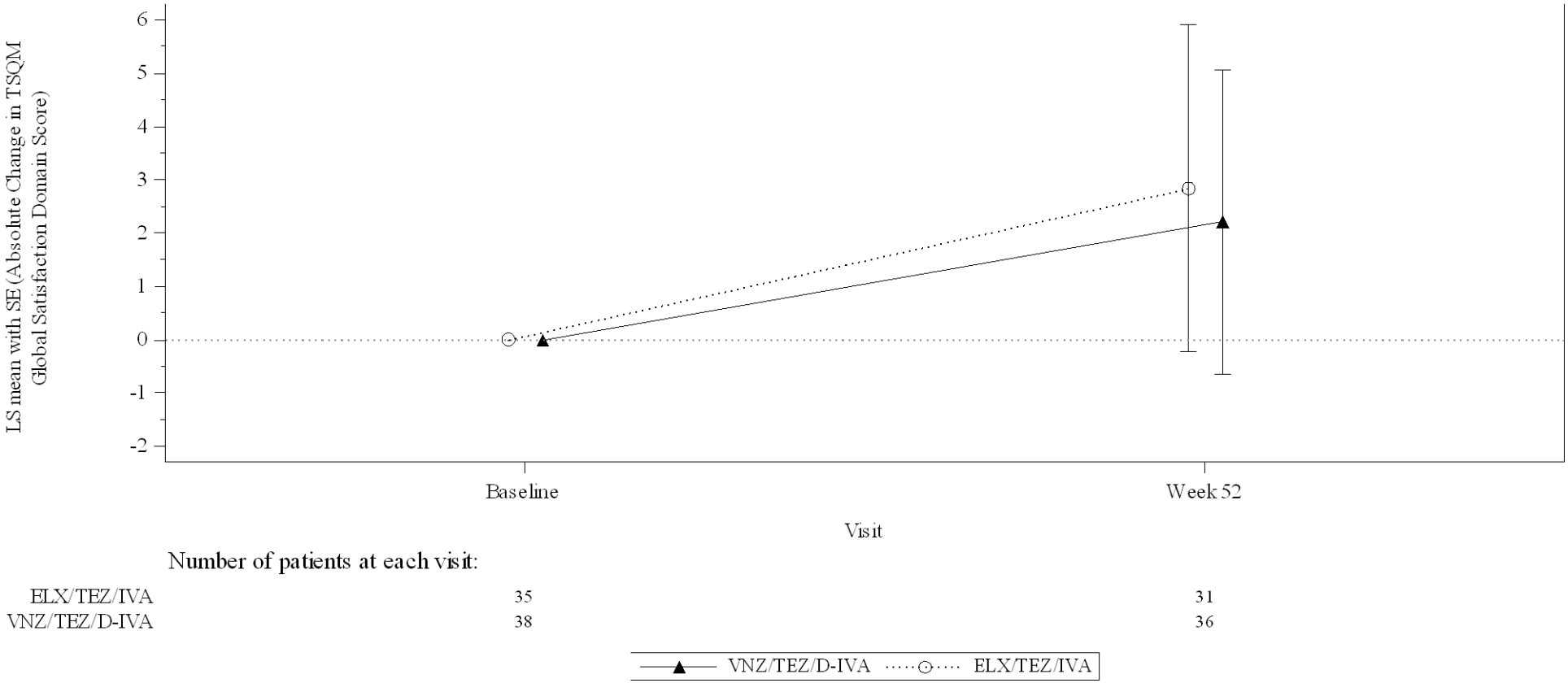
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction



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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-103.sas Creation: 07JAN2025 11:35

Figure 2.2.1.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment

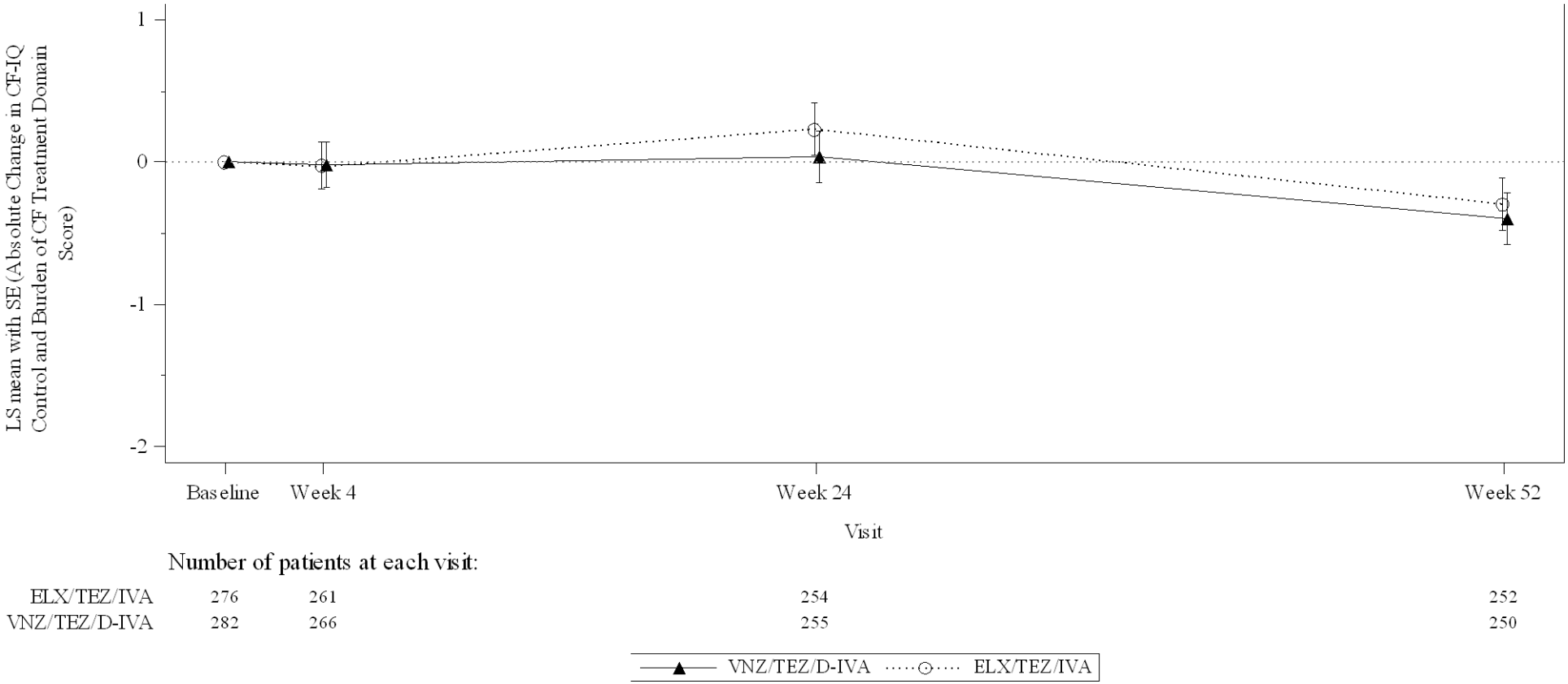

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Figure 2.2.1.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity

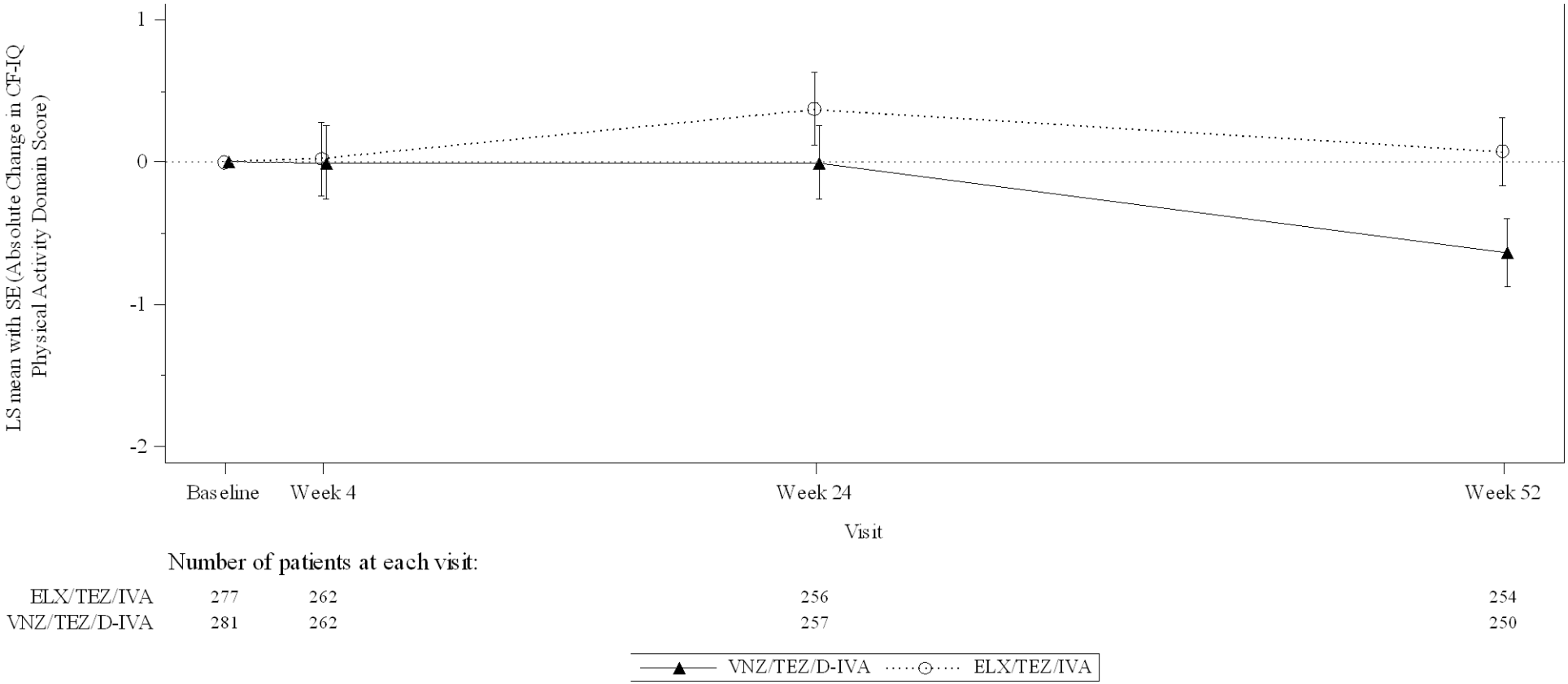

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Figure 2.2.1.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social

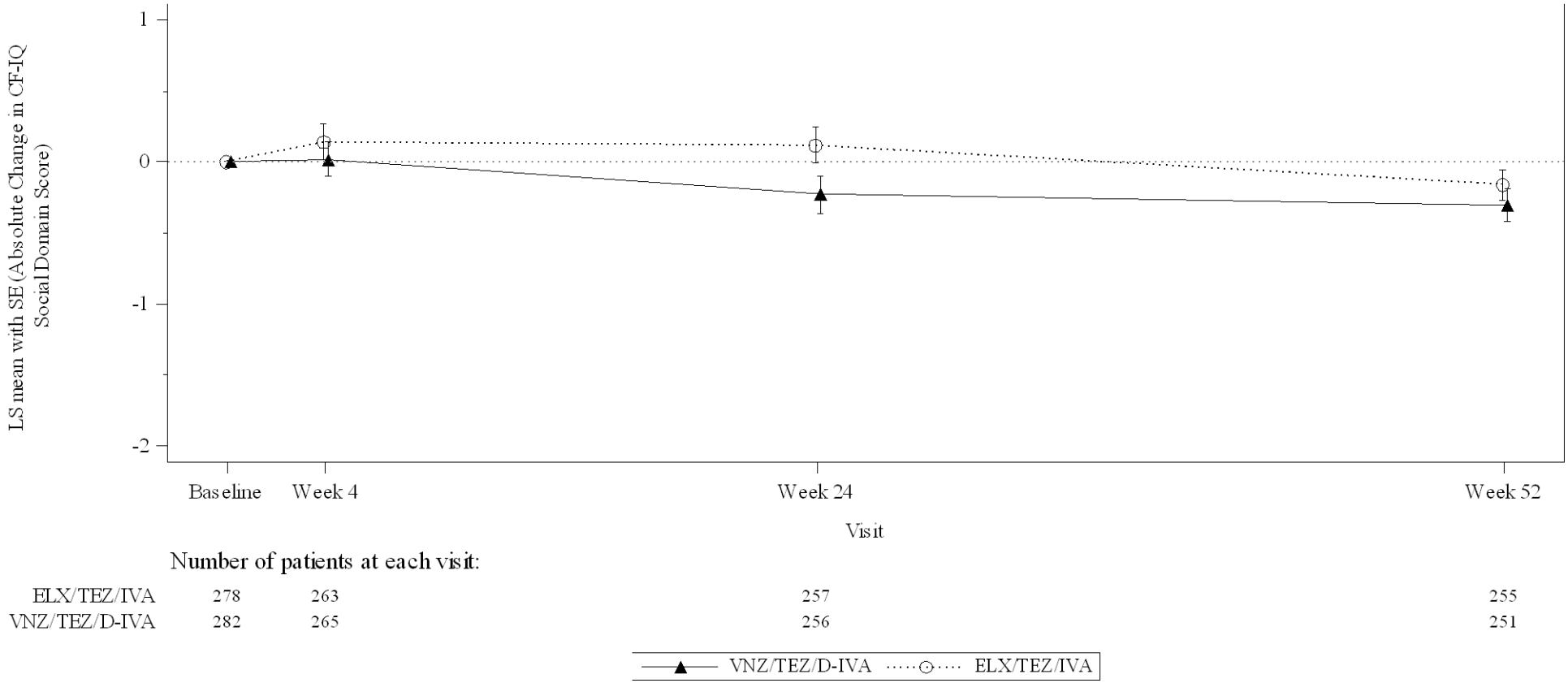

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Figure 2.2.1.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion

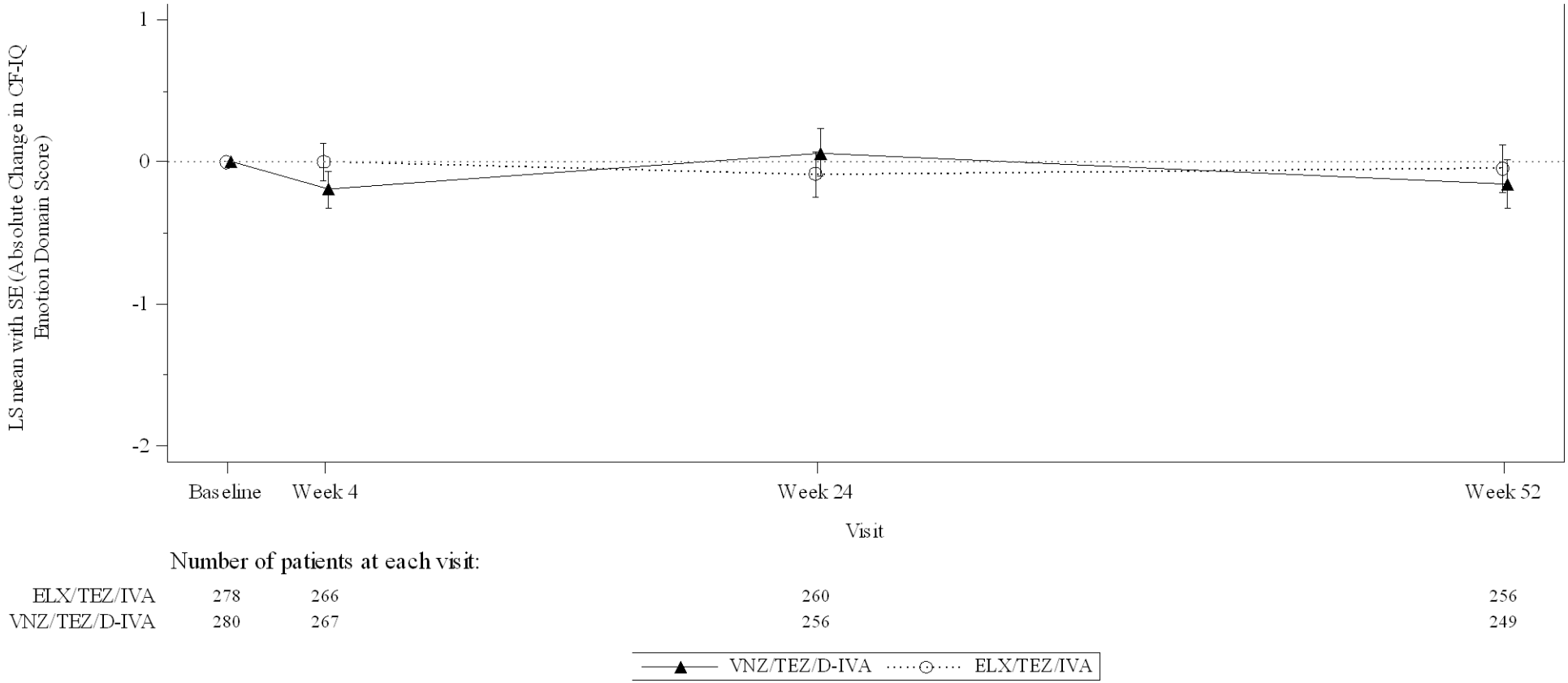

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Figure 2.2.1.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations

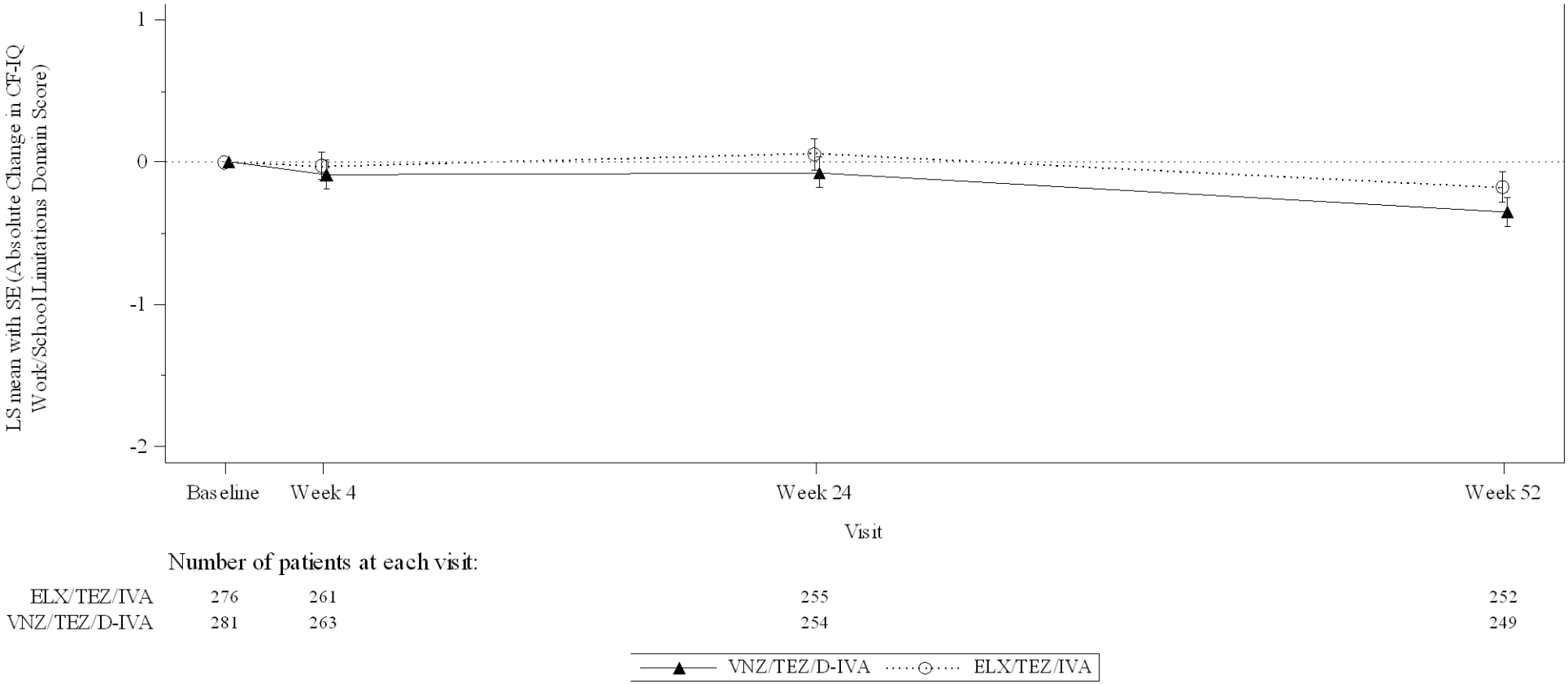

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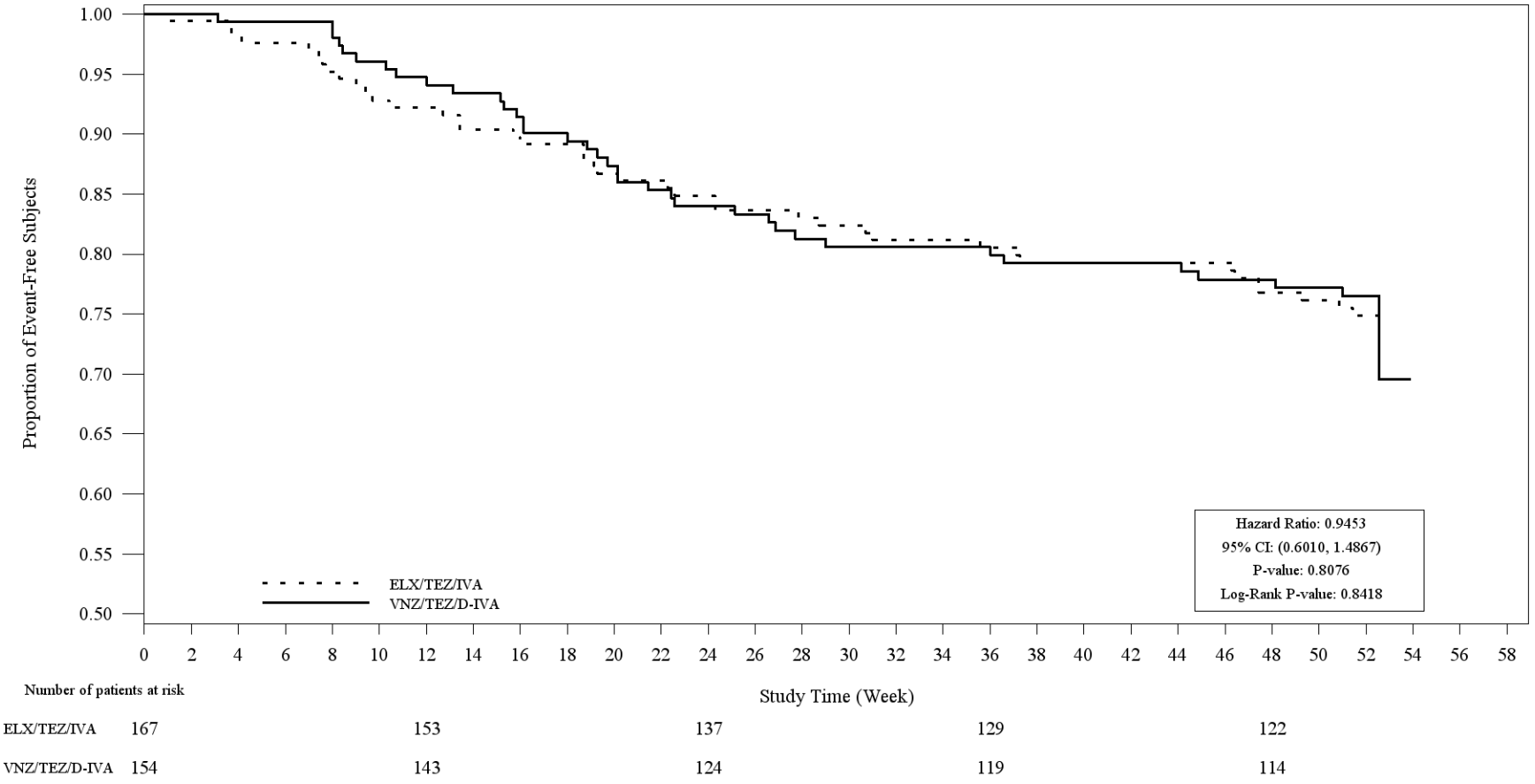
Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: ppFEV$_1$ at Baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

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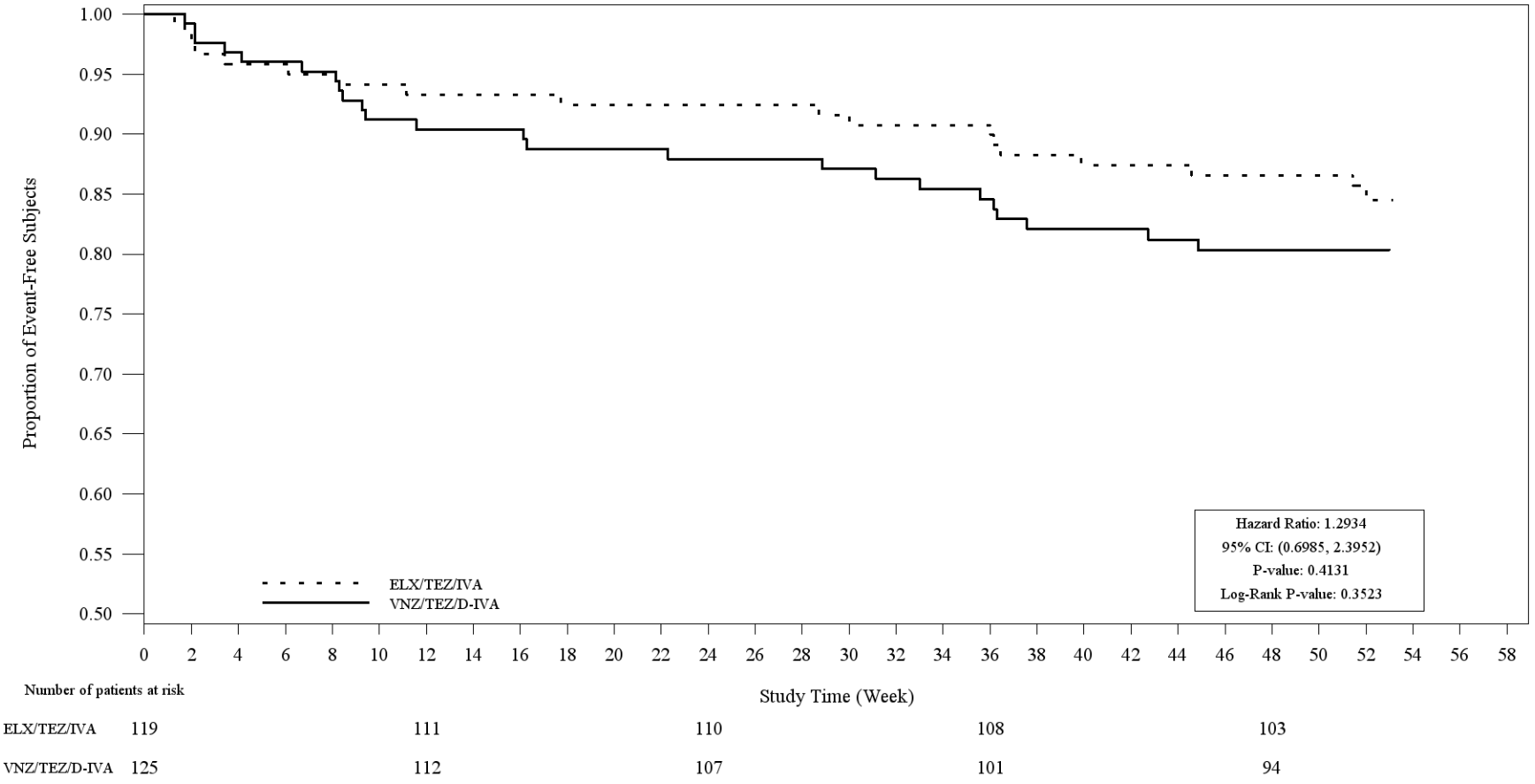
Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: ppFEV$_1$ at Baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

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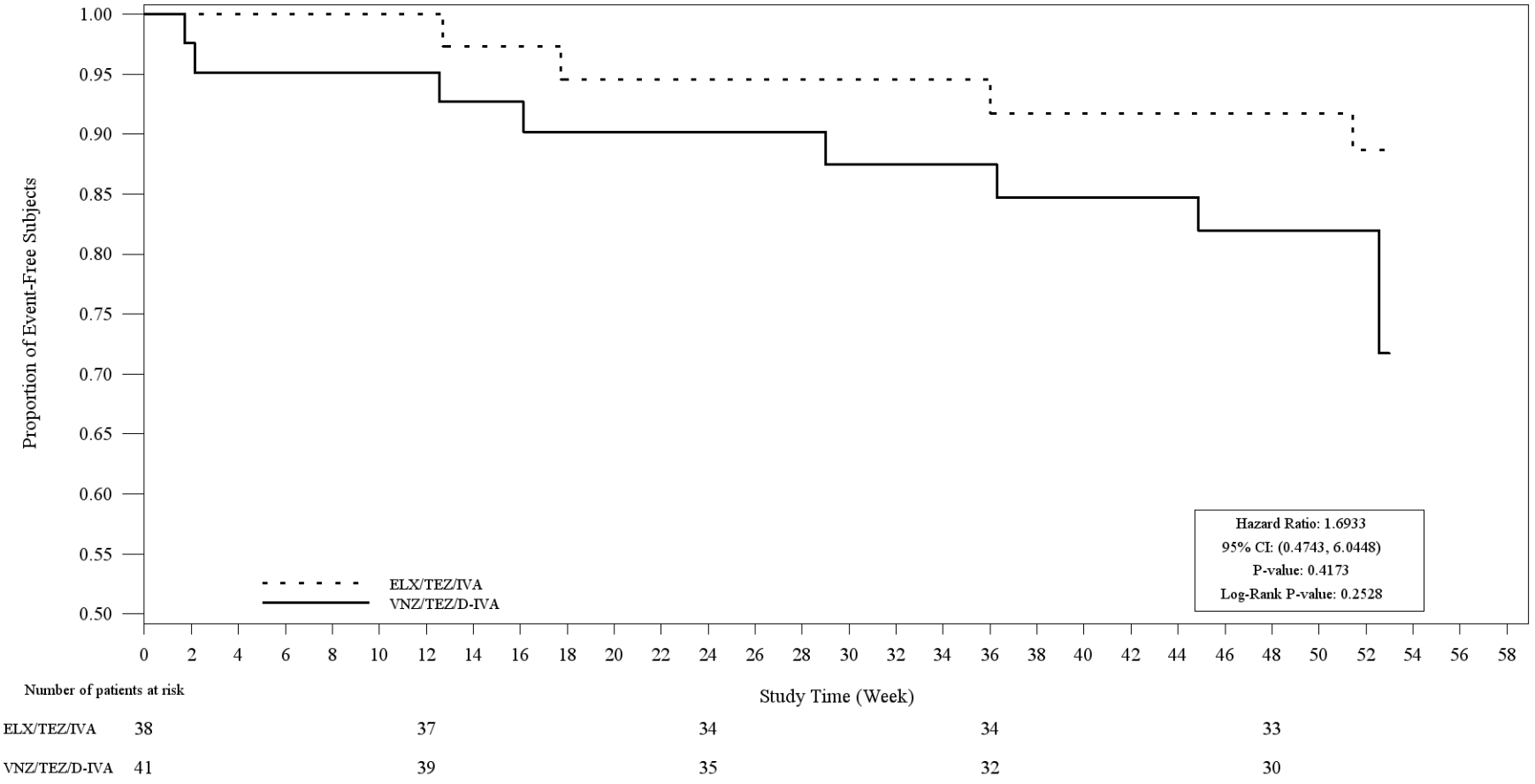
Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening < 18 years



Number of patients at risk

ELX/TEZ/IVA	38	37	34	34	33
VNZ/TEZ/D-IVA	41	39	35	32	30

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

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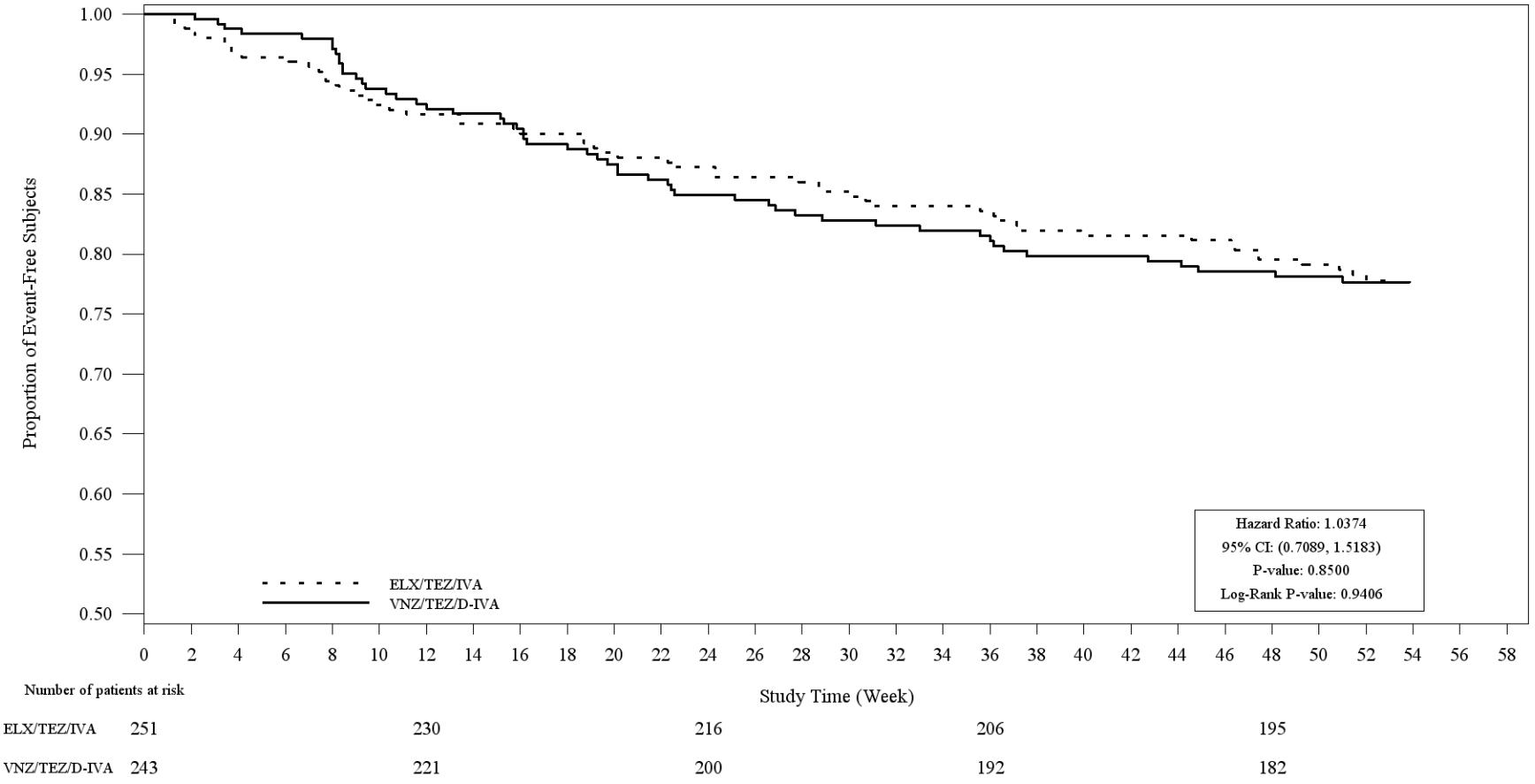
Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening ≥ 18 years



Number of patients at risk

ELX/TEZ/IVA	251	230	216	206	195
VNZ/TEZ/D-IVA	243	221	200	192	182

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

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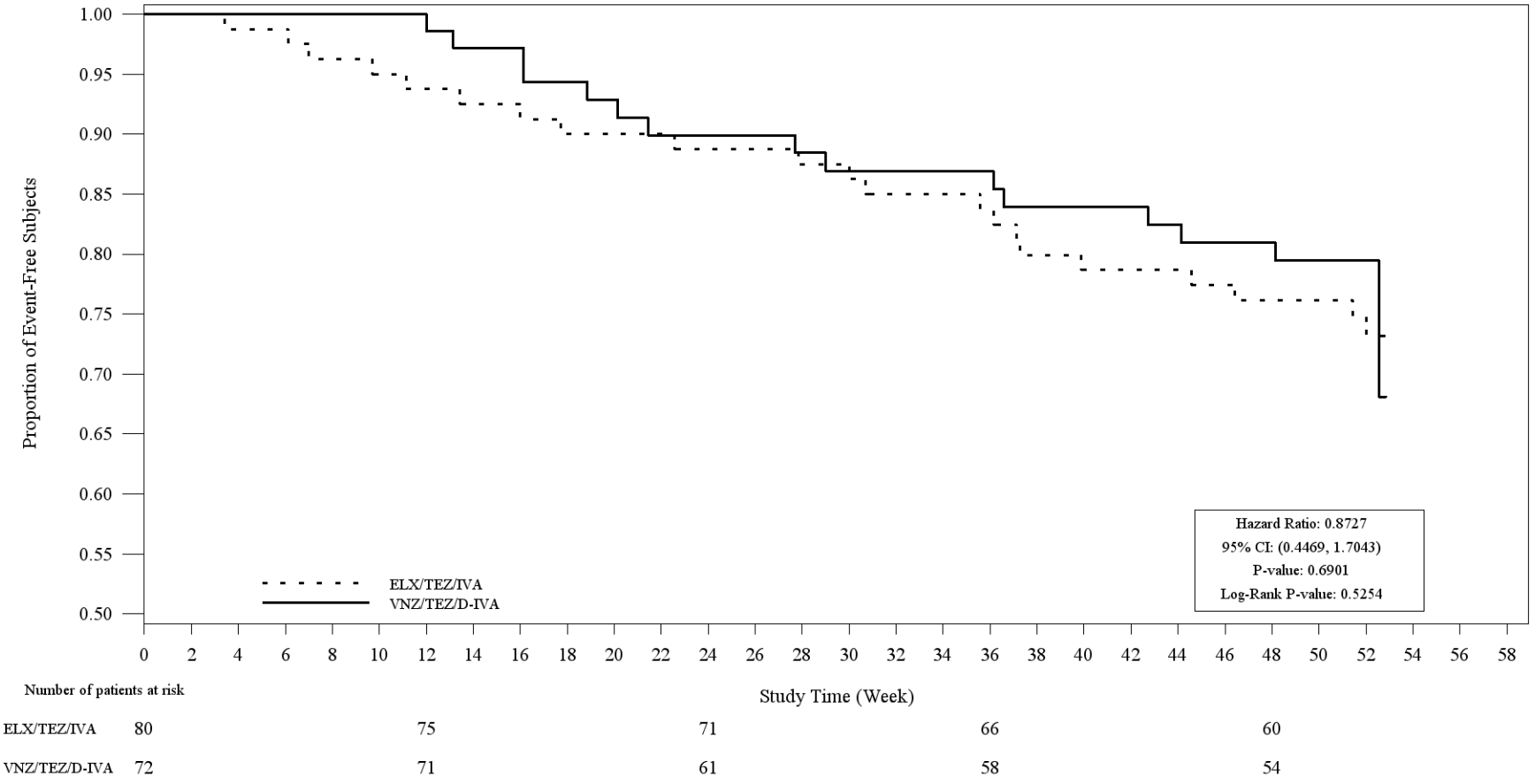
Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline <30 mmol/L

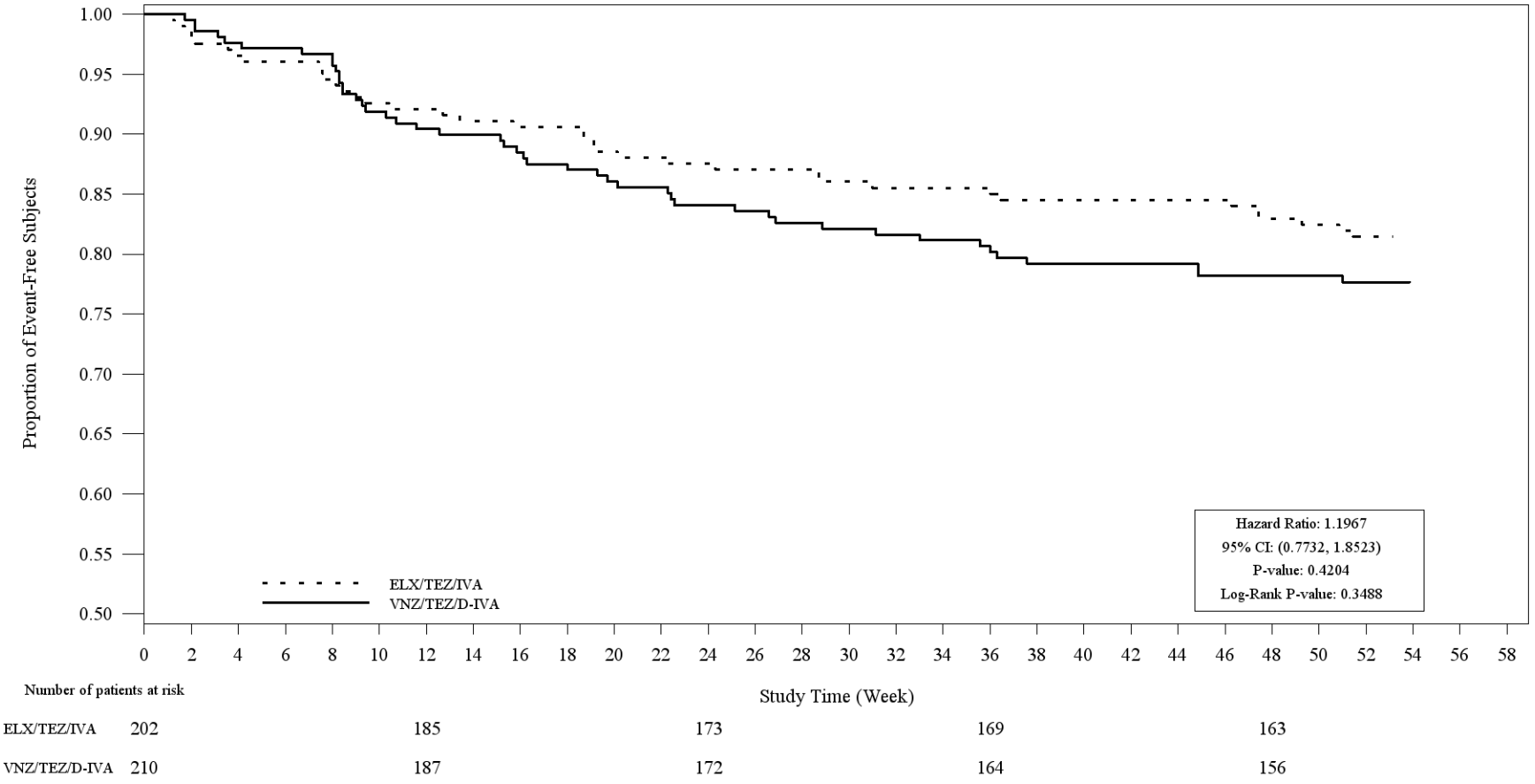


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline ≥30 mmol/L



Number of patients at risk

ELX/TEZ/IVA	202	185	173	169	163
VNZ/TEZ/D-IVA	210	187	172	164	156

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

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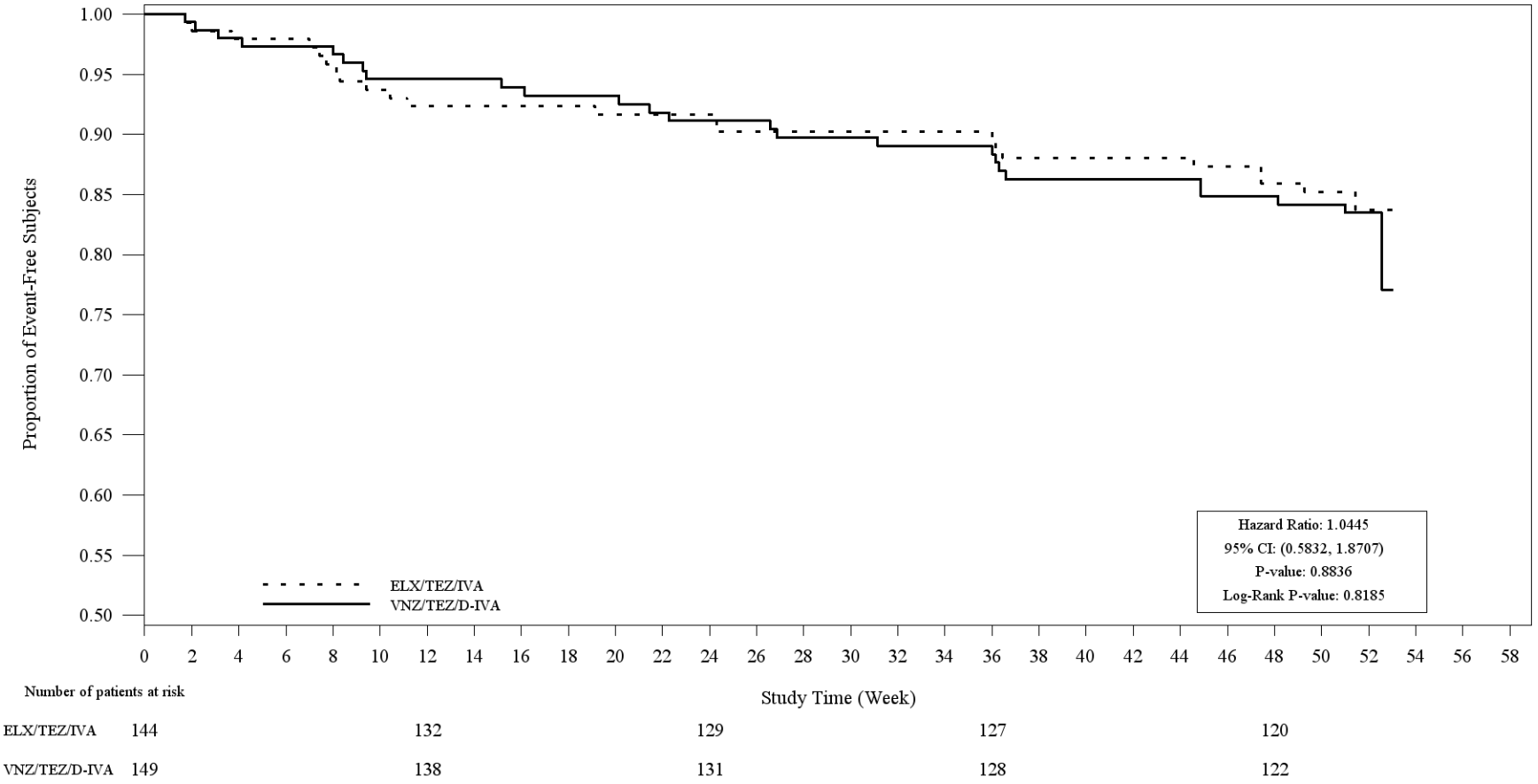
Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Male



Number of patients at risk

ELX/TEZ/IVA	144	132	129	127	120
VNZ/TEZ/D-IVA	149	138	131	128	122

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

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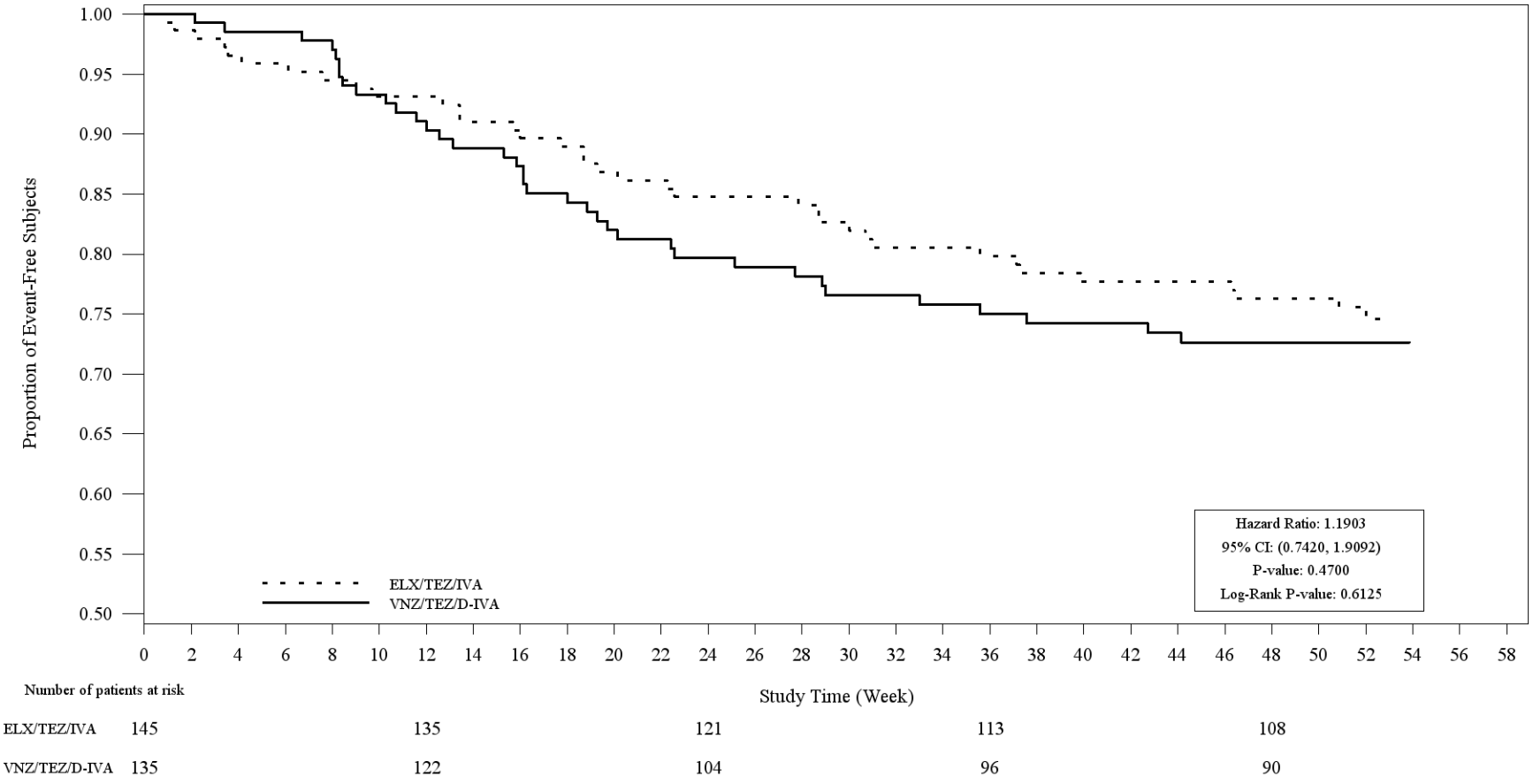
Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Female



Number of patients at risk

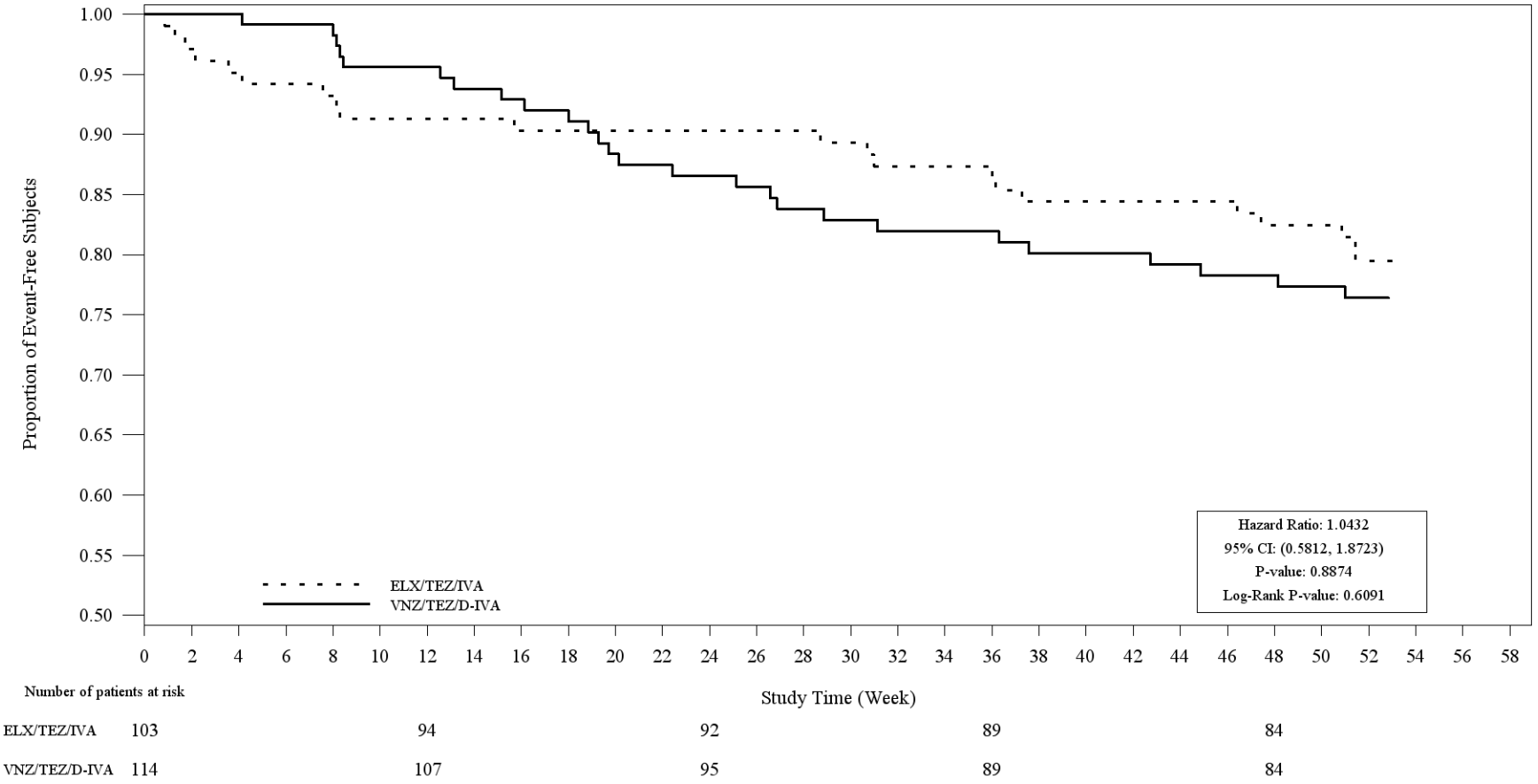
ELX/TEZ/IVA	145	135	121	113	108
VNZ/TEZ/D-IVA	135	122	104	96	90

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = North America



Number of patients at risk

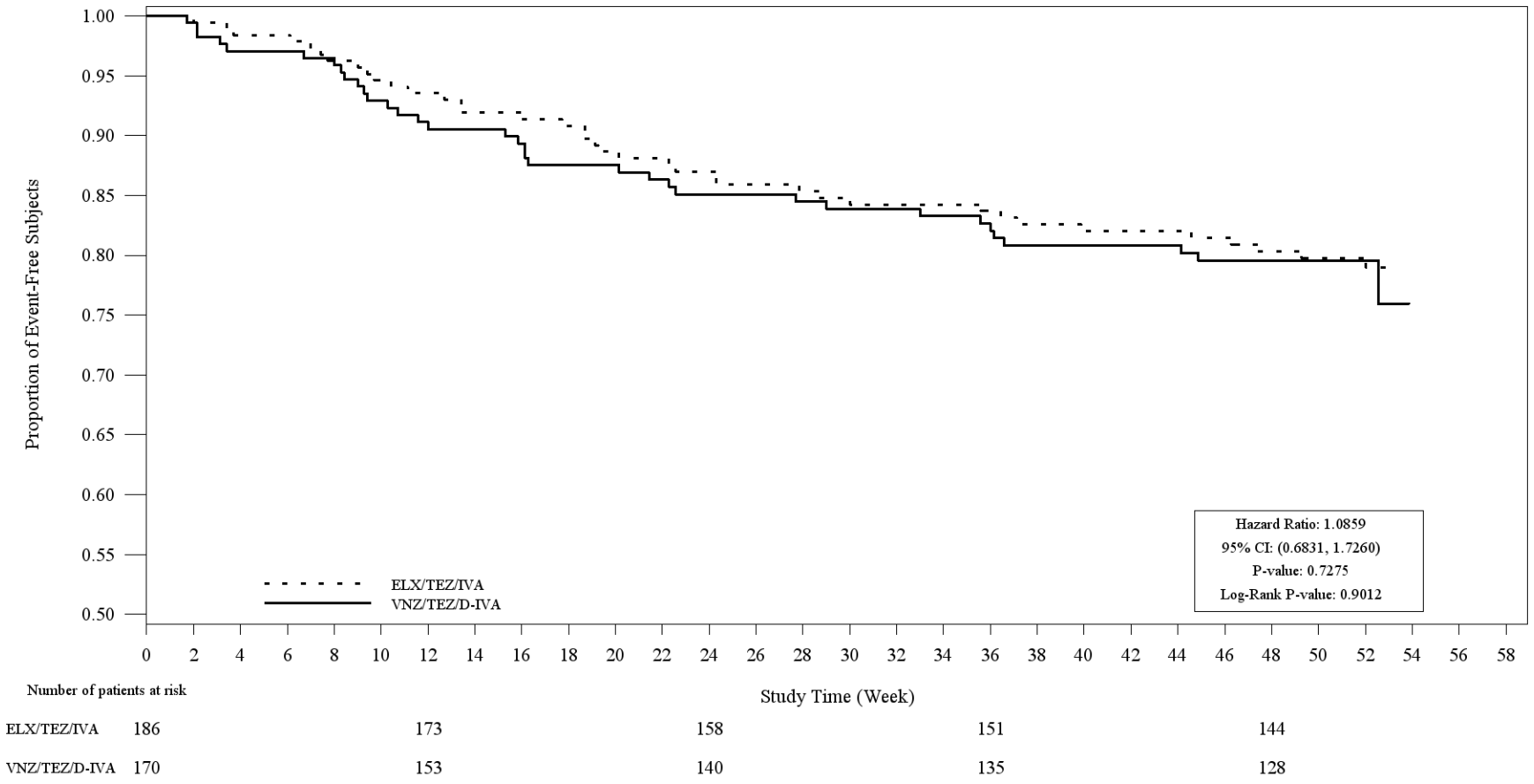
ELX/TEZ/IVA	103	94	92	89	84
VNZ/TEZ/D-IVA	114	107	95	89	84

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = Rest of the World



Number of patients at risk

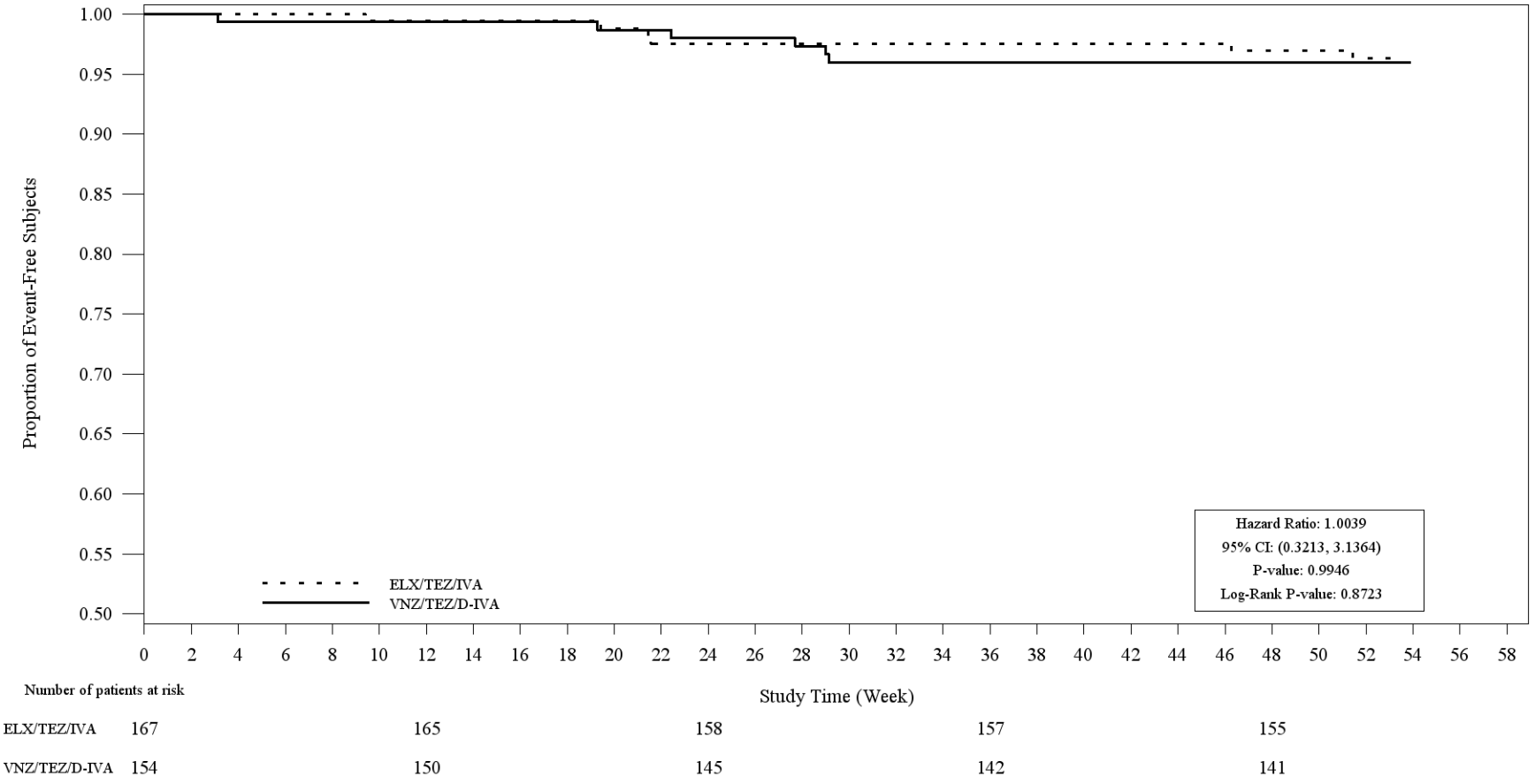
ELX/TEZ/IVA	186	173	158	151	144
VNZ/TEZ/D-IVA	170	153	140	135	128

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: ppFEV$_1$ at Baseline <70 %



Number of patients at risk

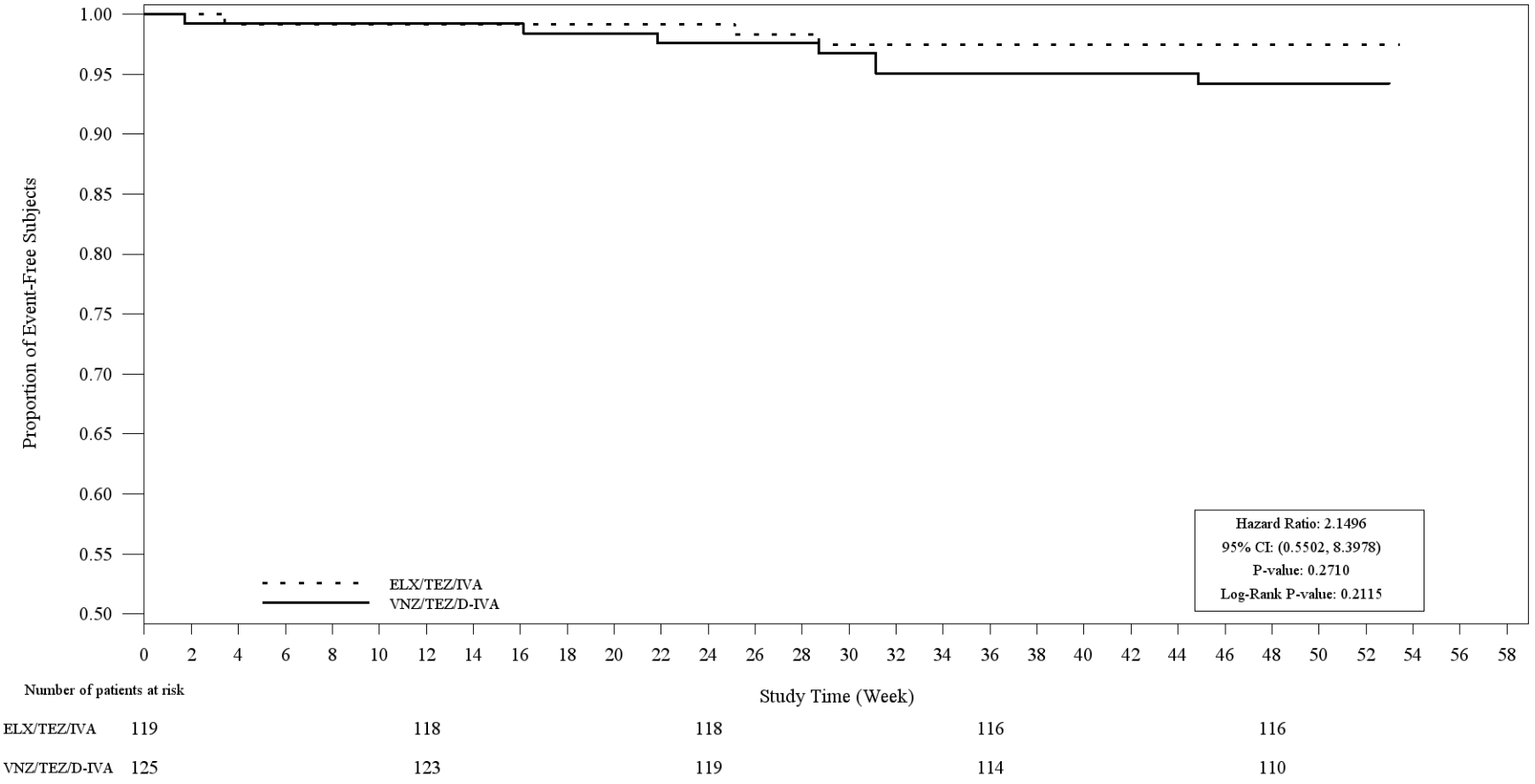
ELX/TEZ/IVA	167	165	158	157	155
VNZ/TEZ/D-IVA	154	150	145	142	141

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-hosp-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: ppFEV$_1$ at Baseline ≥70 %

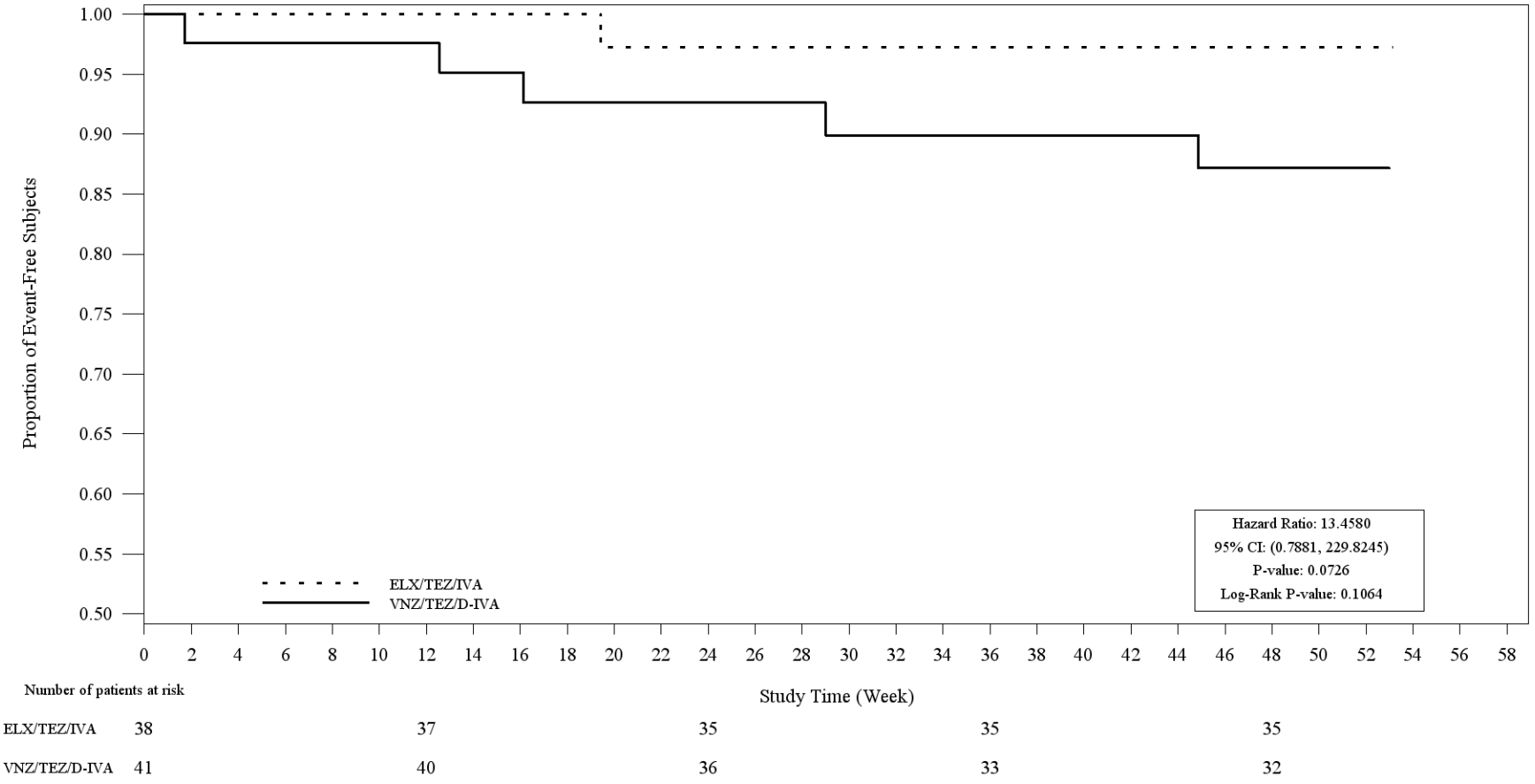


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-hosp-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening < 18 years

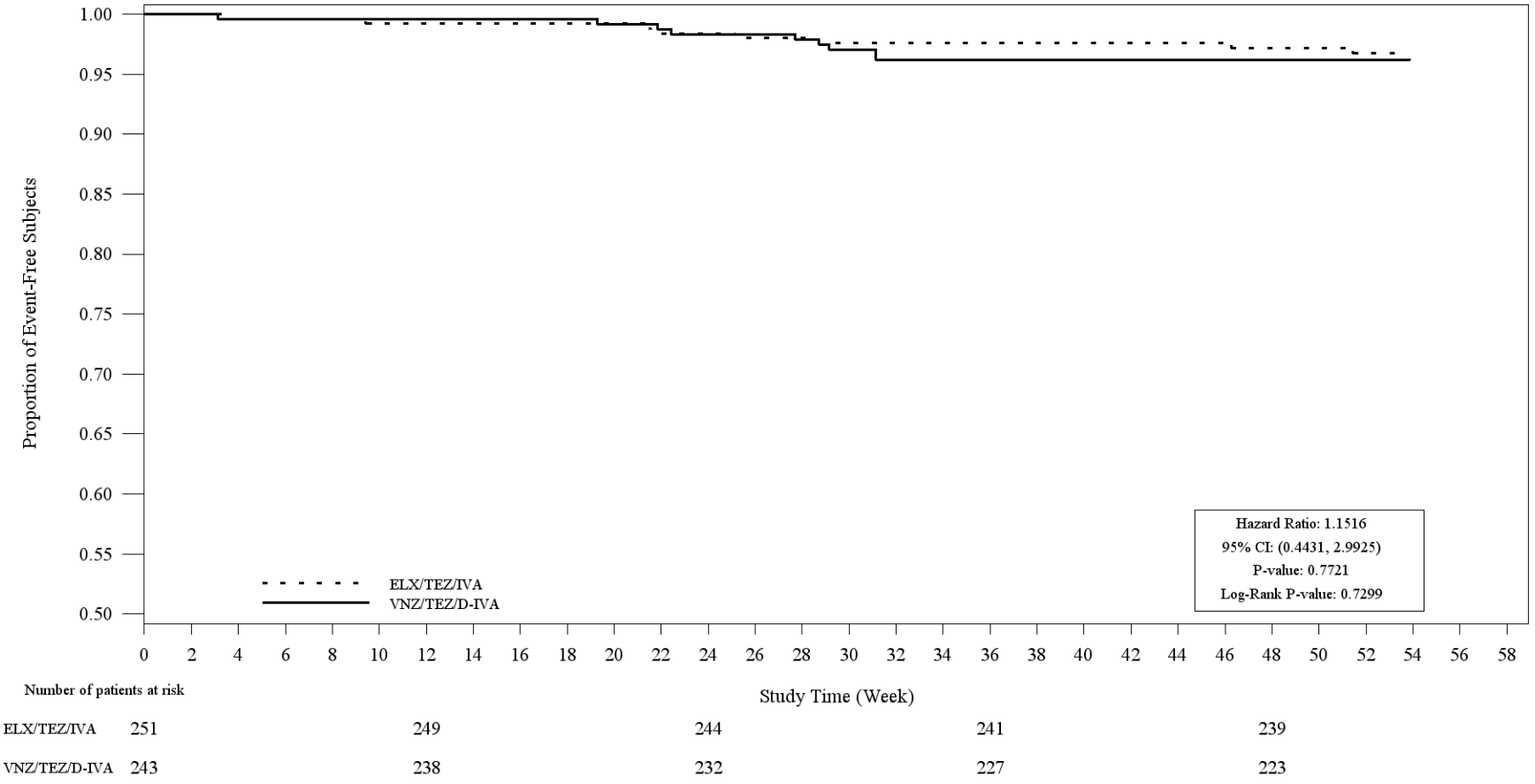


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-hosp-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening ≥ 18 years



Number of patients at risk

ELX/TEZ/IVA	251	249	244	241	239
VNZ/TEZ/D-IVA	243	238	232	227	223

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

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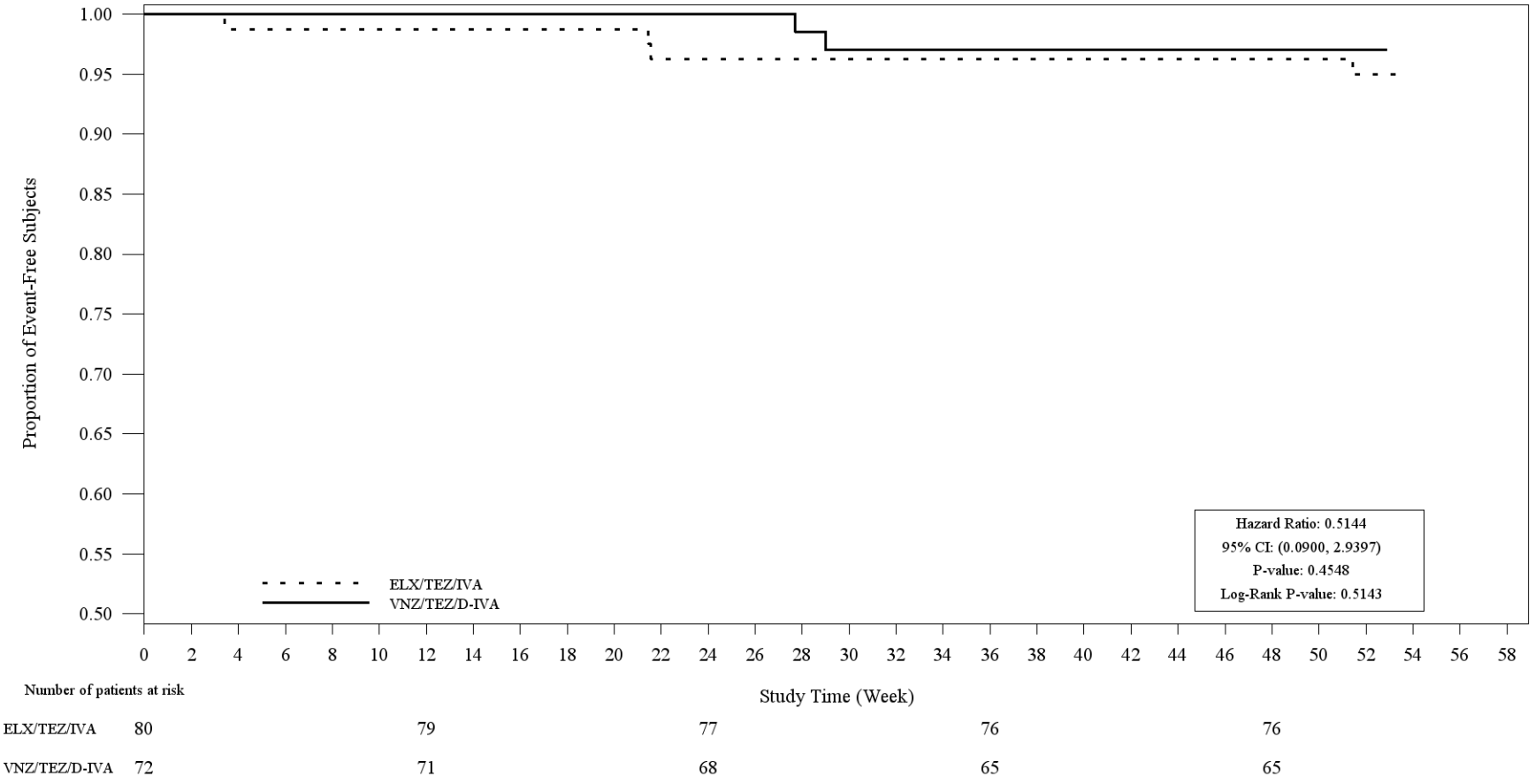
Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline <30 mmol/L

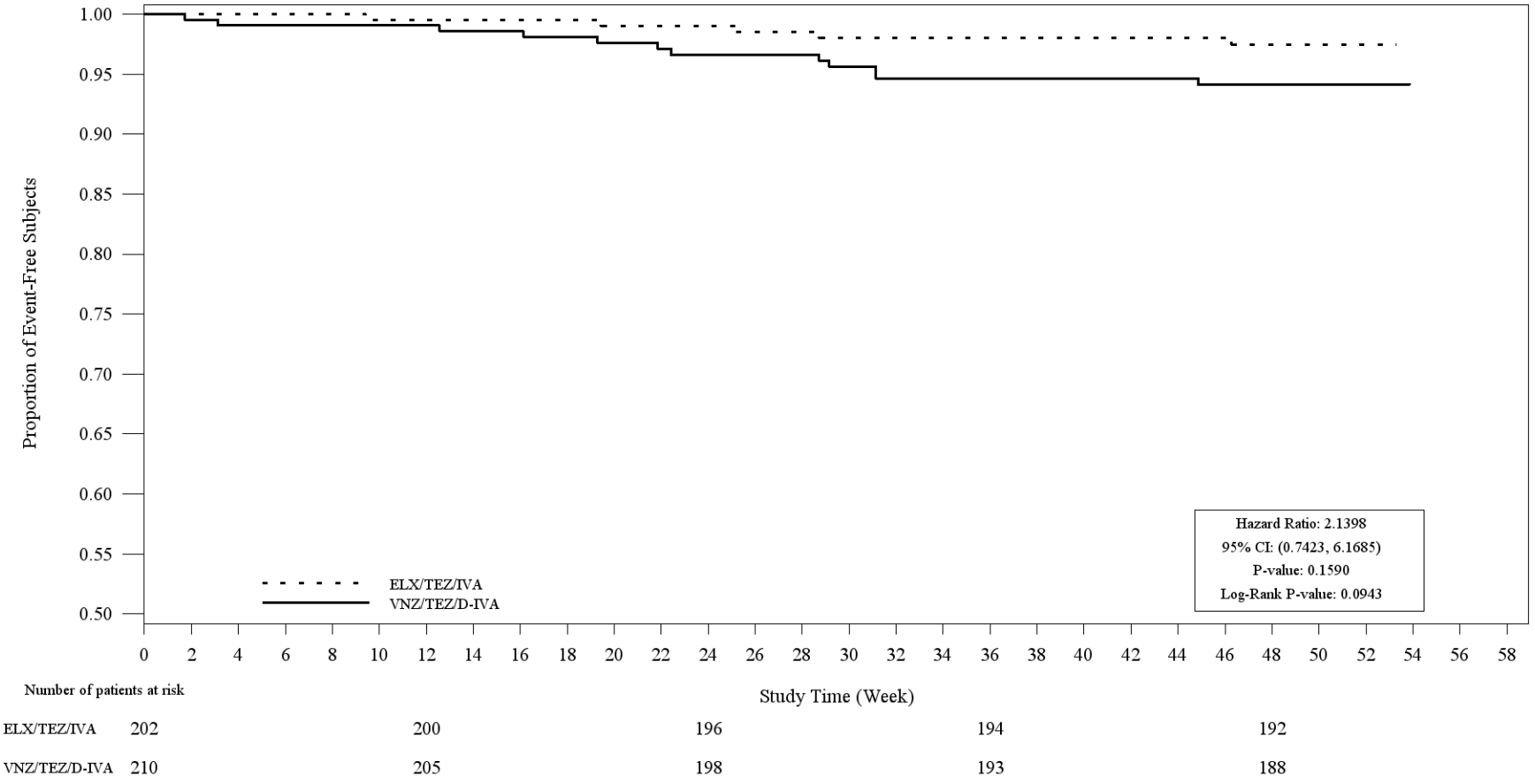


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-hosp-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline ≥30 mmol/L



Number of patients at risk

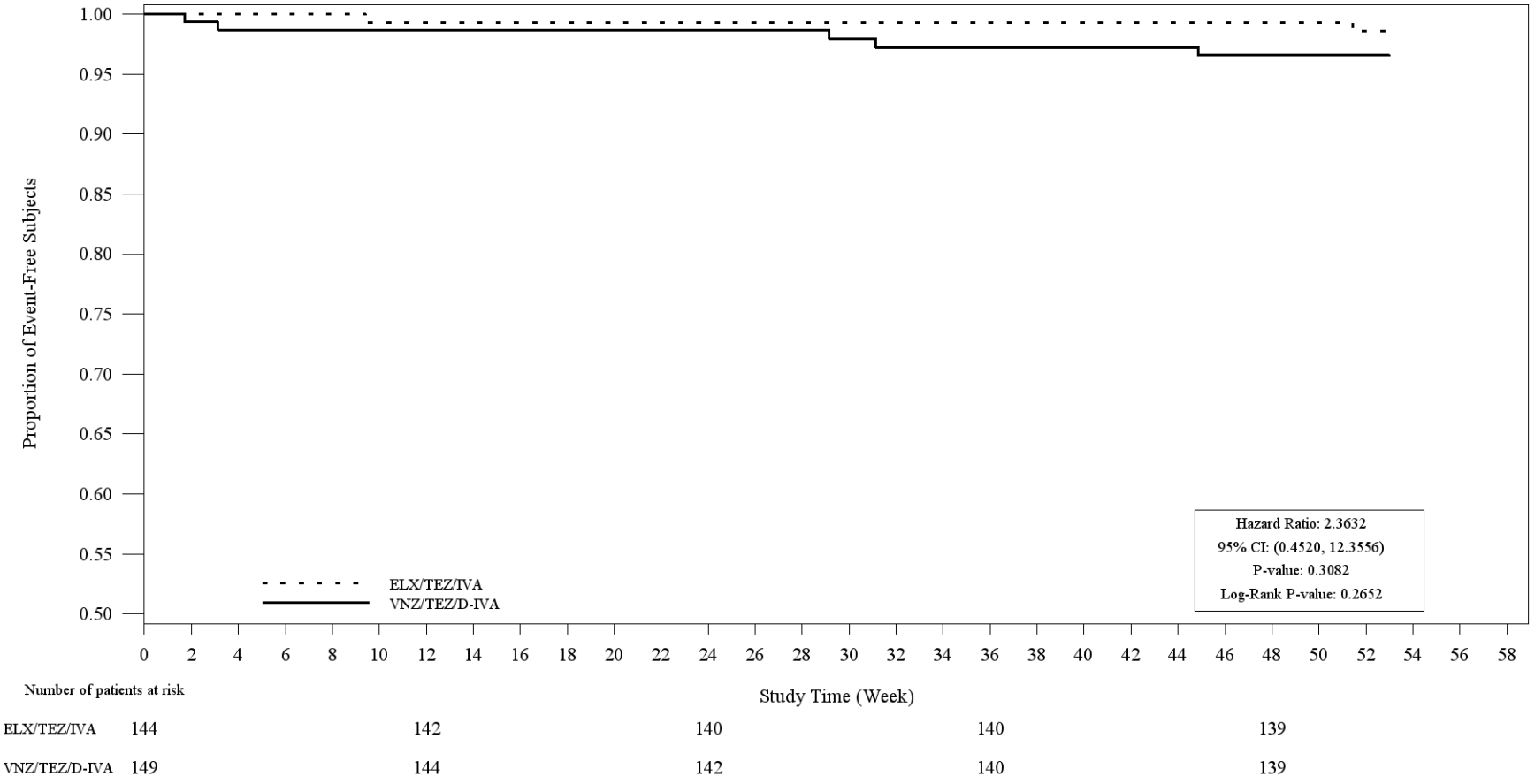
ELX/TEZ/IVA	202	200	196	194	192
VNZ/TEZ/D-IVA	210	205	198	193	188

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-hosp-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Male

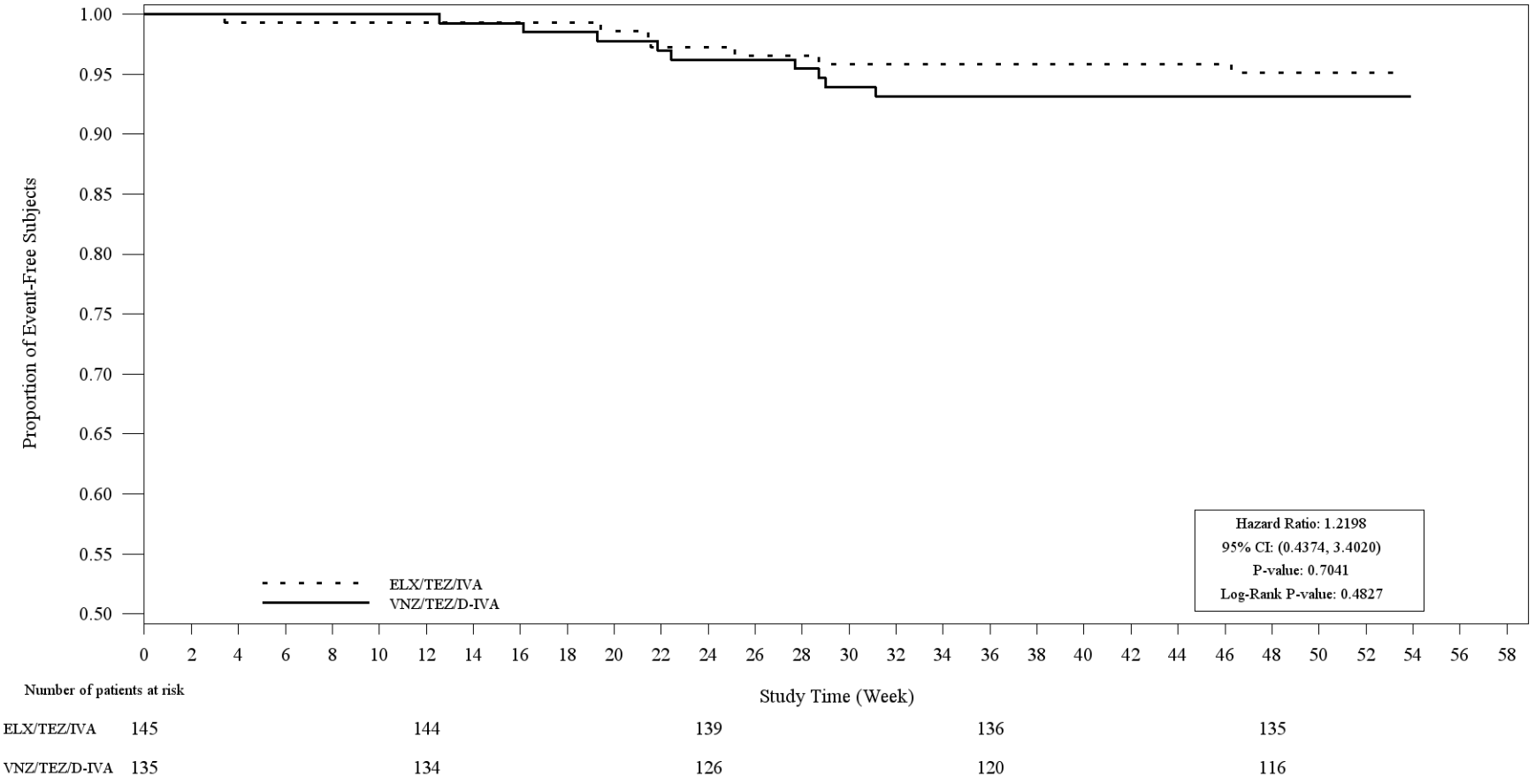


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-hosp-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Female



Number of patients at risk

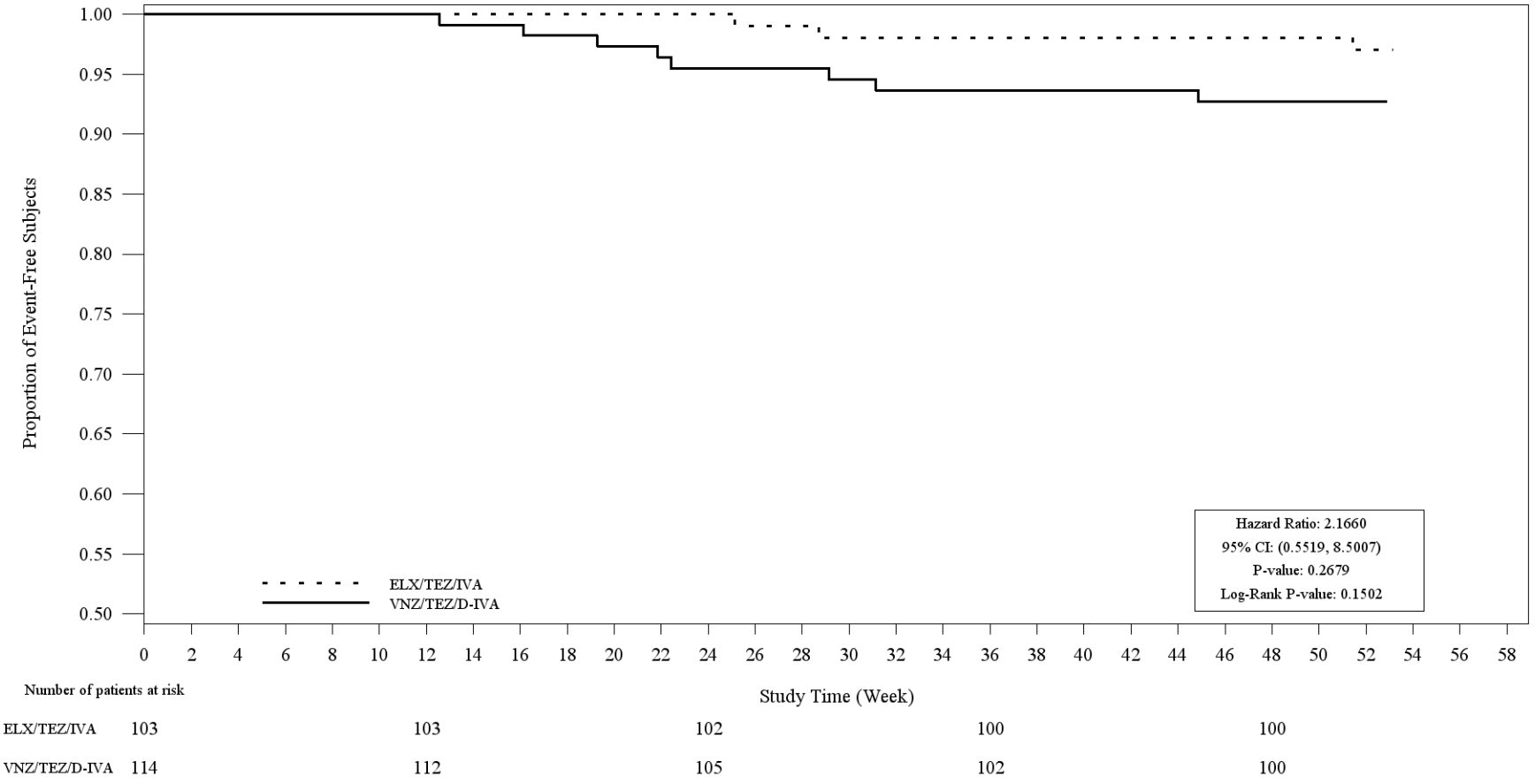
ELX/TEZ/IVA	145	144	139	136	135
VNZ/TEZ/D-IVA	135	134	126	120	116

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-hosp-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = North America



Number of patients at risk

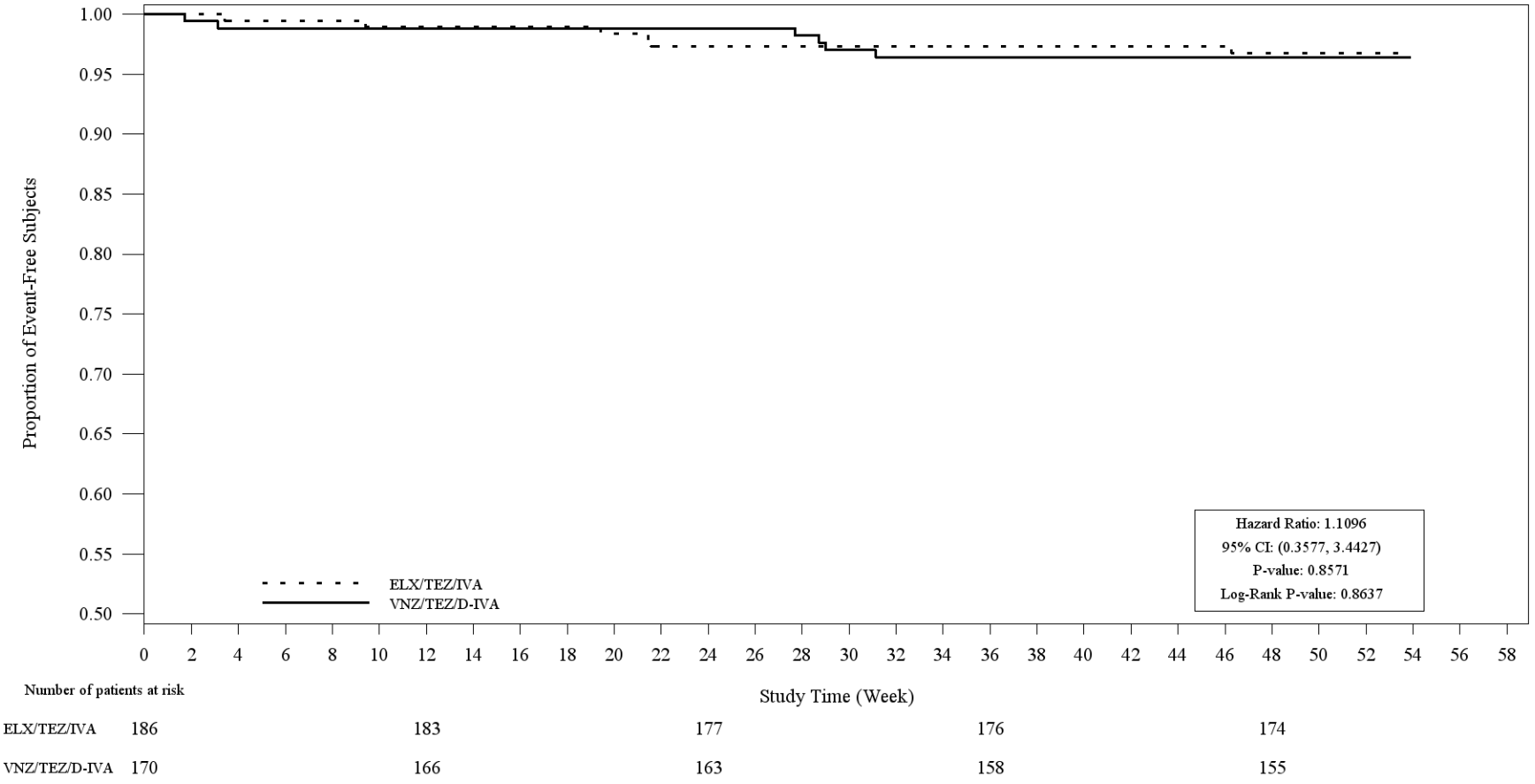
ELX/TEZ/IVA	103	103	102	100	100
VNZ/TEZ/D-IVA	114	112	105	102	100

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-hosp-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = Rest of the World

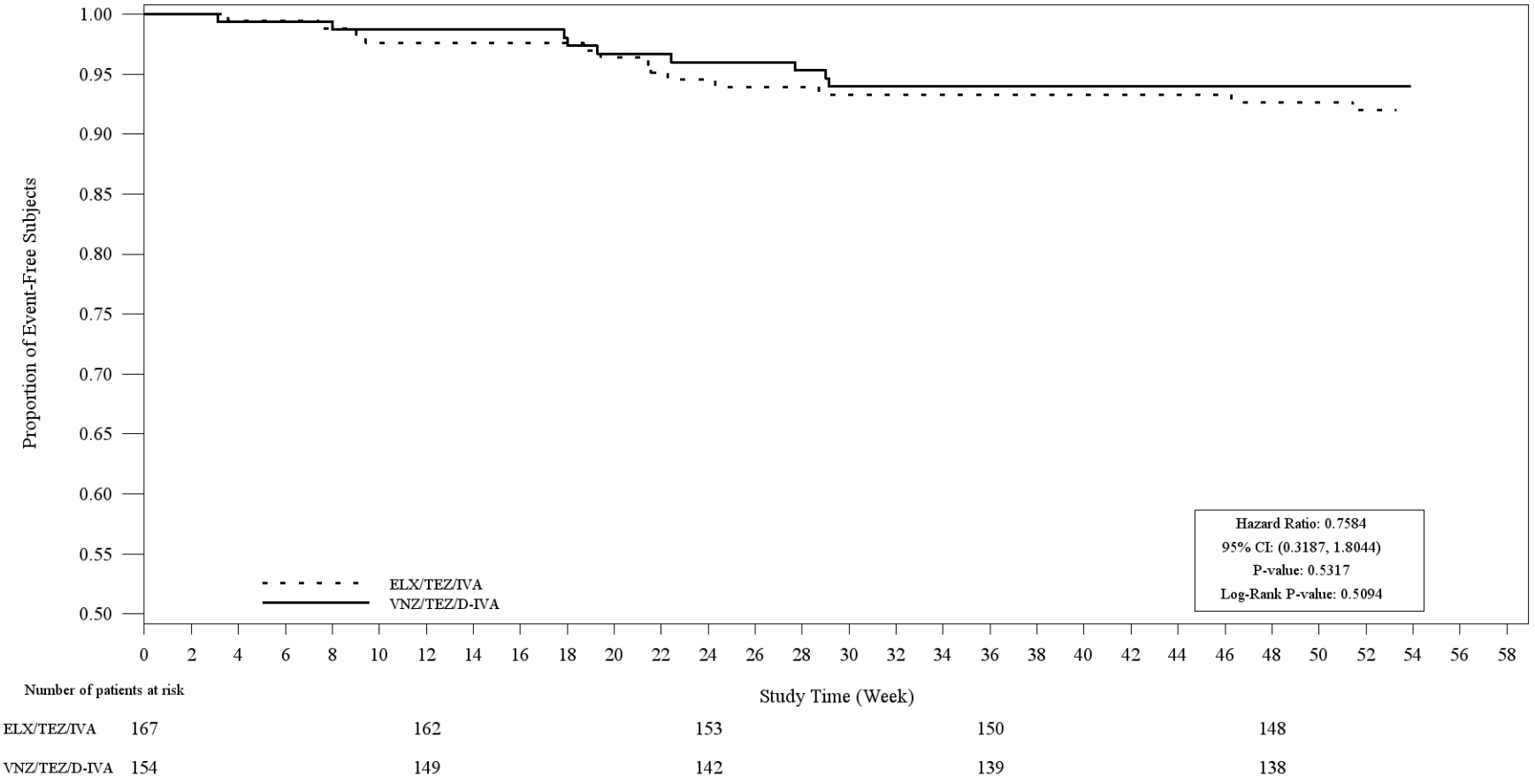


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-hosp-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: ppFEV$_1$ at Baseline <70 %

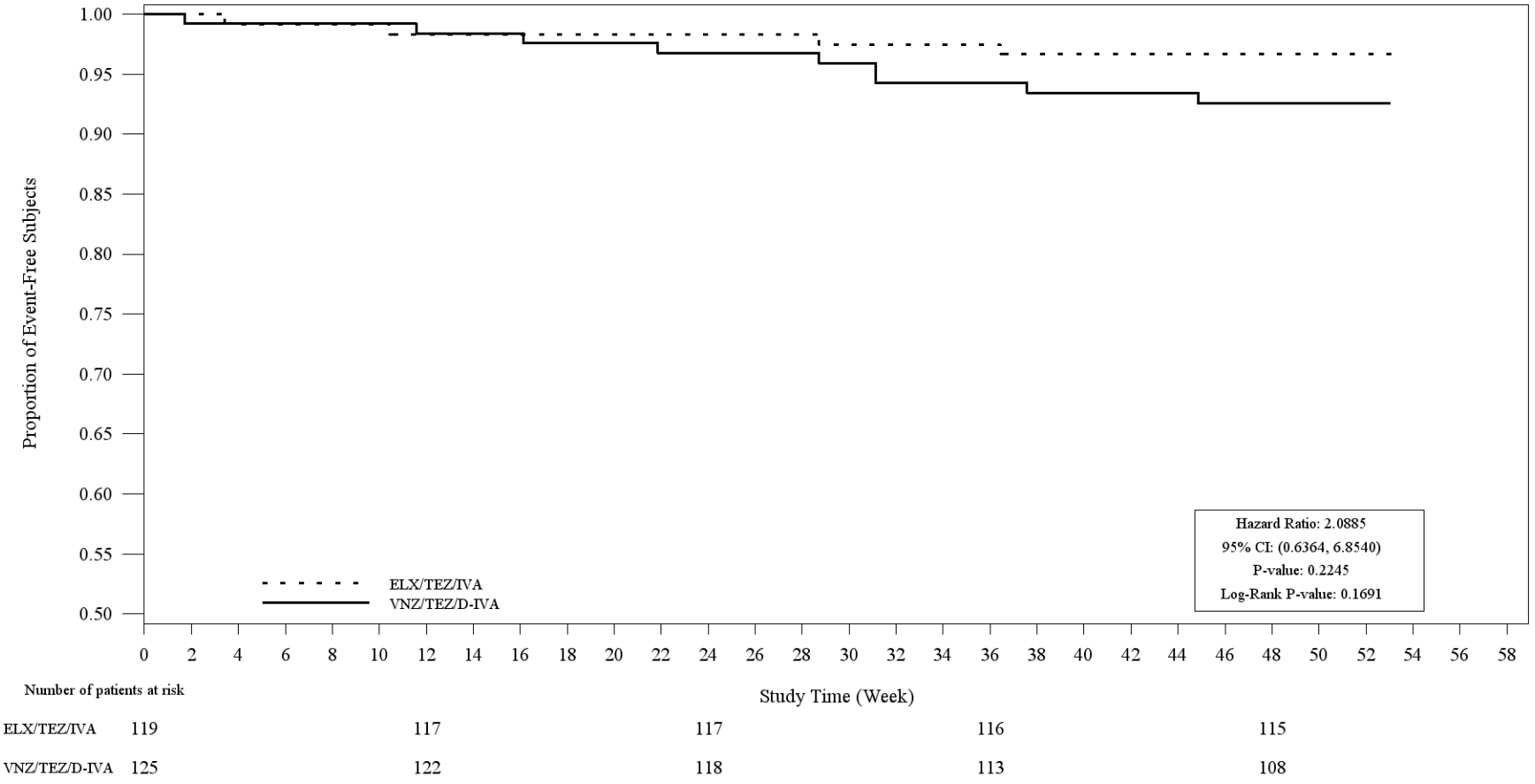


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-iv-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: ppFEV$_1$ at Baseline ≥70 %

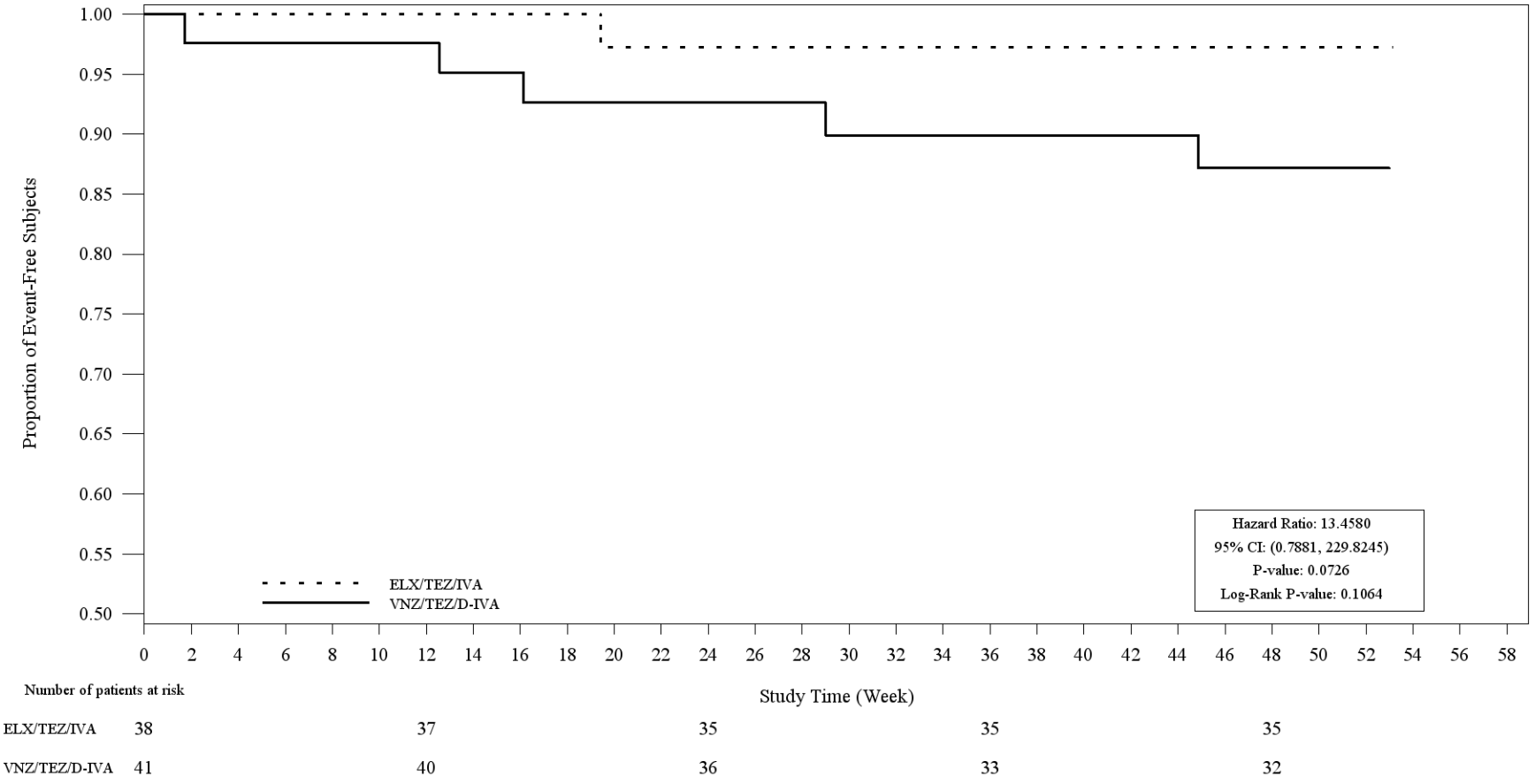


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-iv-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening < 18 years



Number of patients at risk

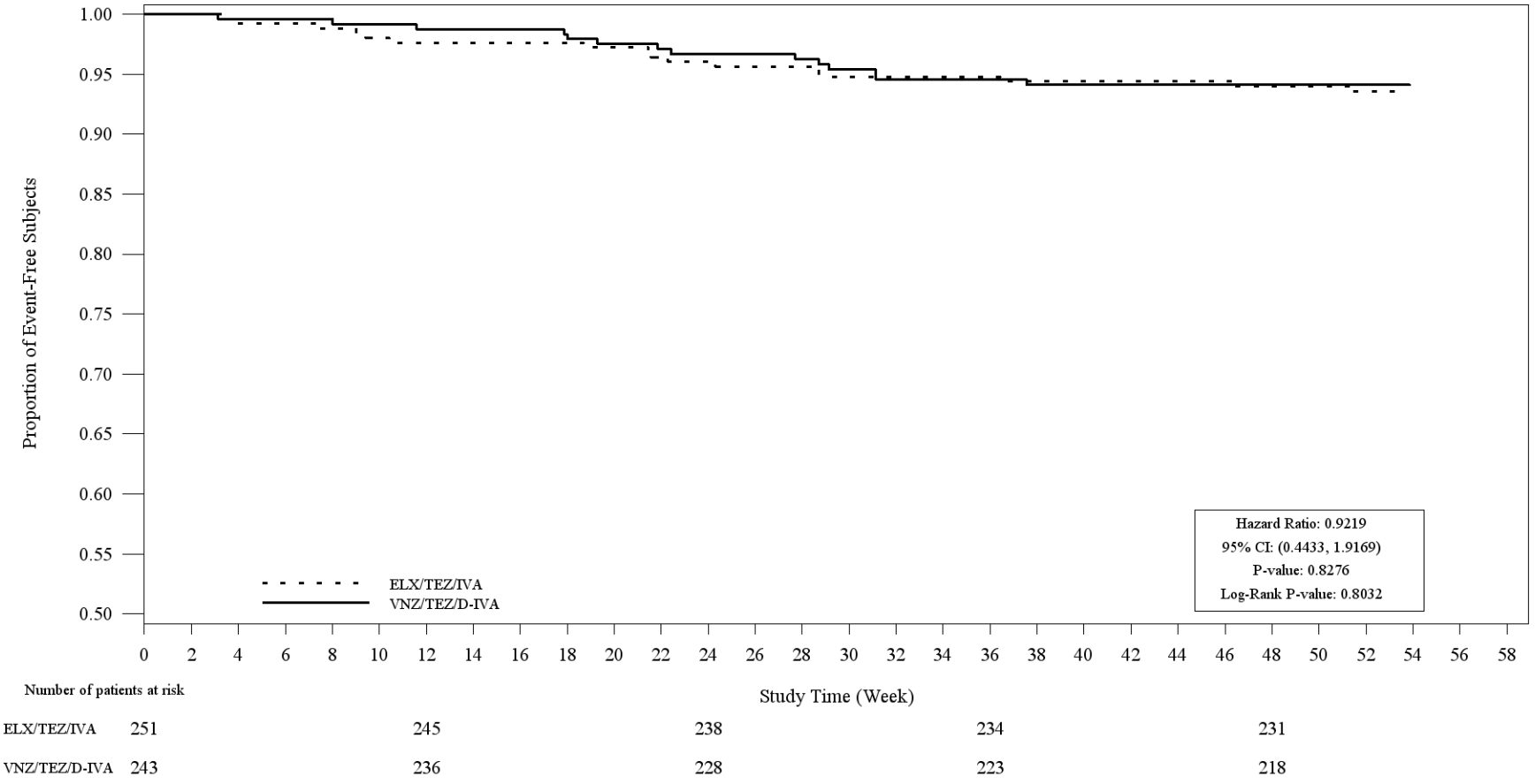
ELX/TEZ/IVA	38	37	35	35	35
VNZ/TEZ/D-IVA	41	40	36	33	32

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-iv-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening ≥ 18 years



Number of patients at risk

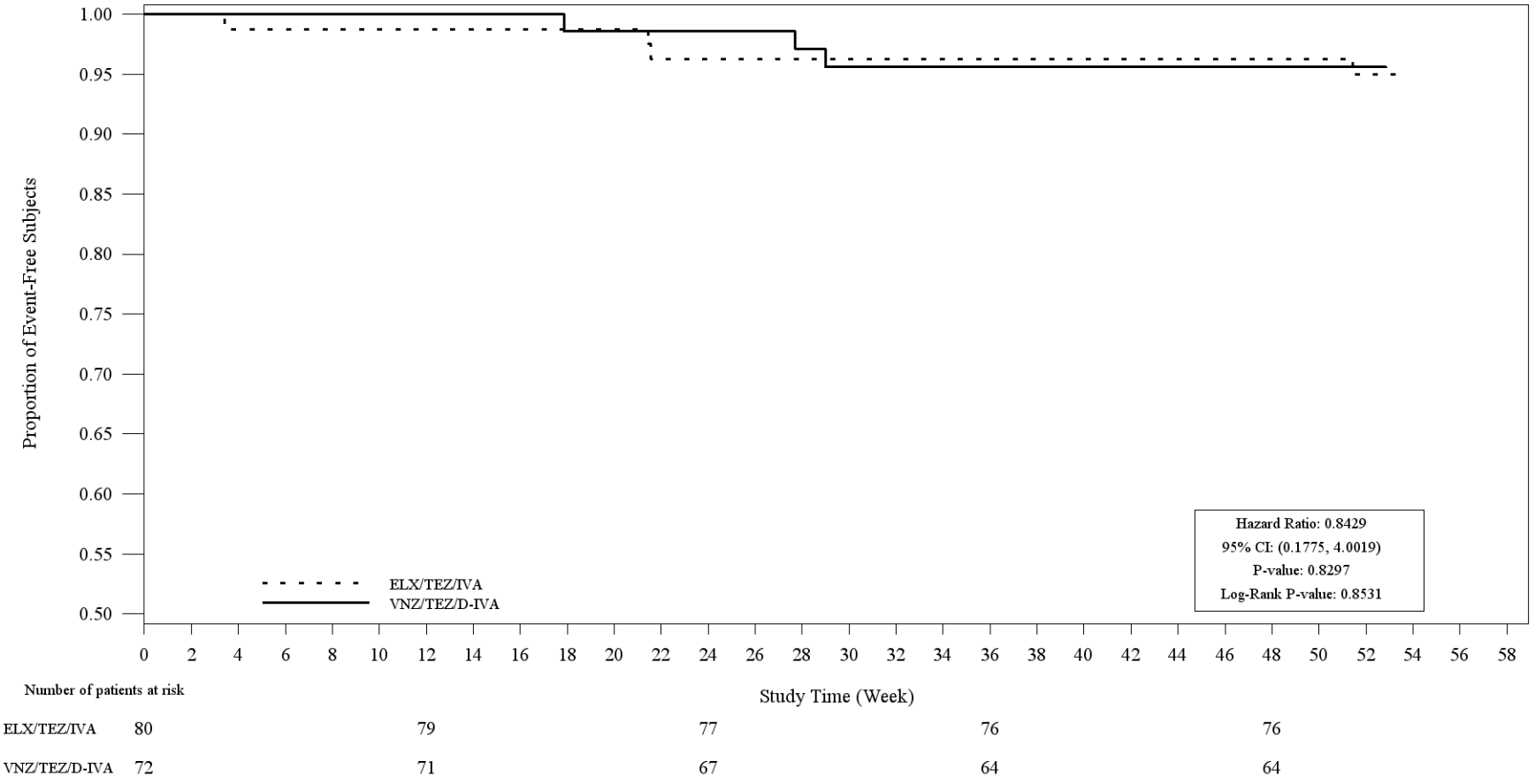
ELX/TEZ/IVA	251	245	238	234	231
VNZ/TEZ/D-IVA	243	236	228	223	218

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-iv-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline <30 mmol/L



Number of patients at risk

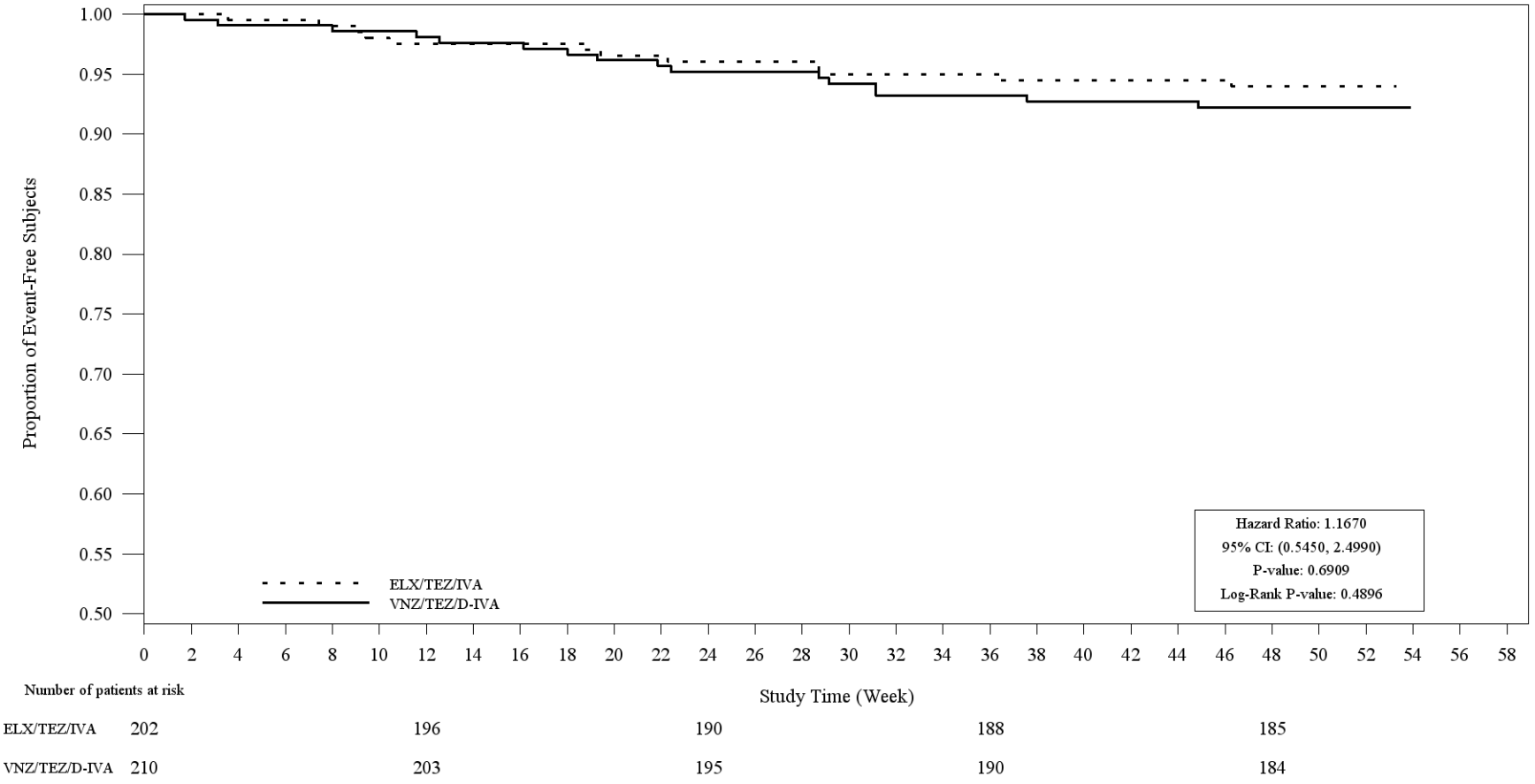
ELX/TEZ/IVA	80	79	77	76	76
VNZ/TEZ/D-IVA	72	71	67	64	64

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-iv-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline ≥30 mmol/L



Number of patients at risk

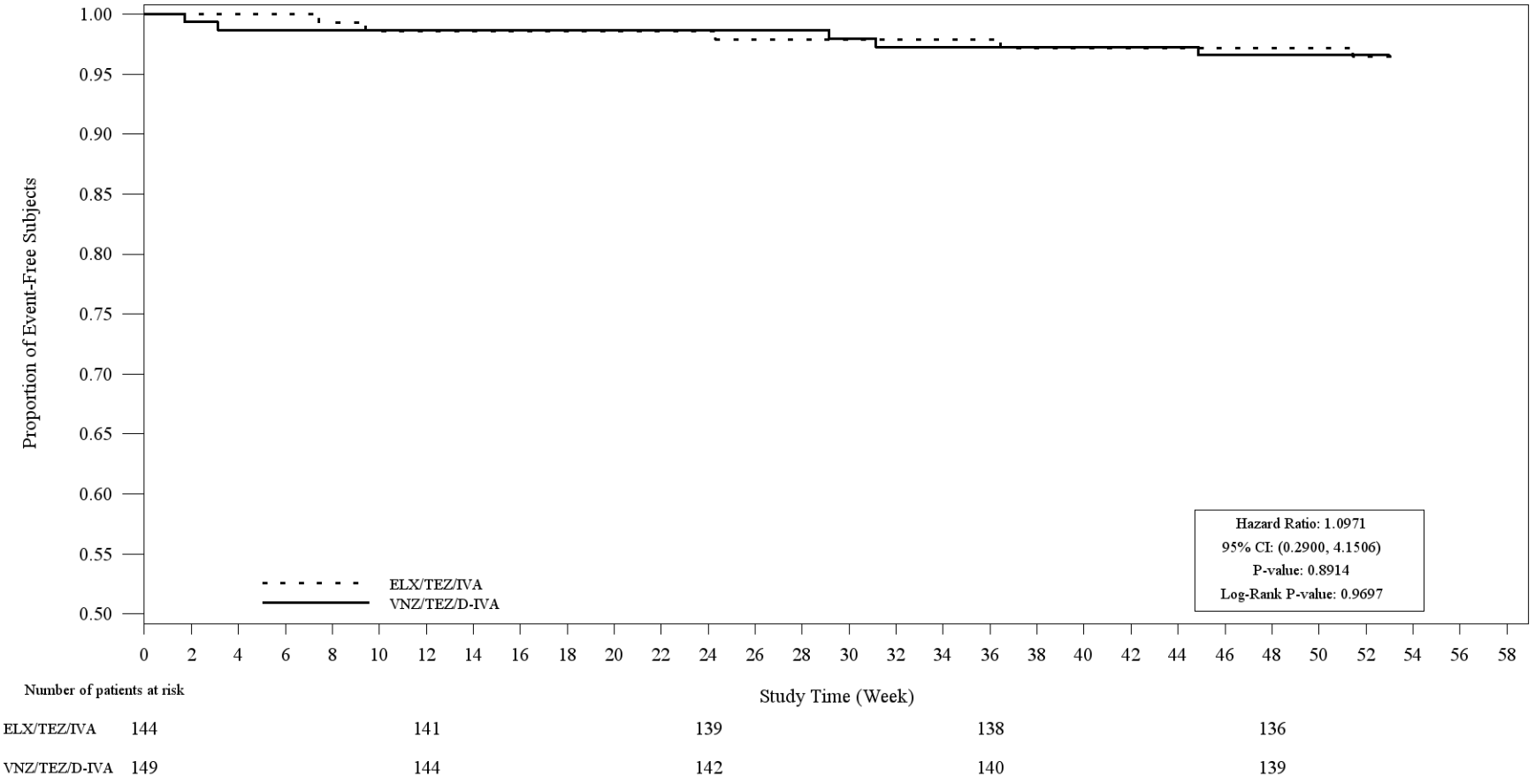
ELX/TEZ/IVA	202	196	190	188	185
VNZ/TEZ/D-IVA	210	203	195	190	184

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-iv-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Male



Number of patients at risk

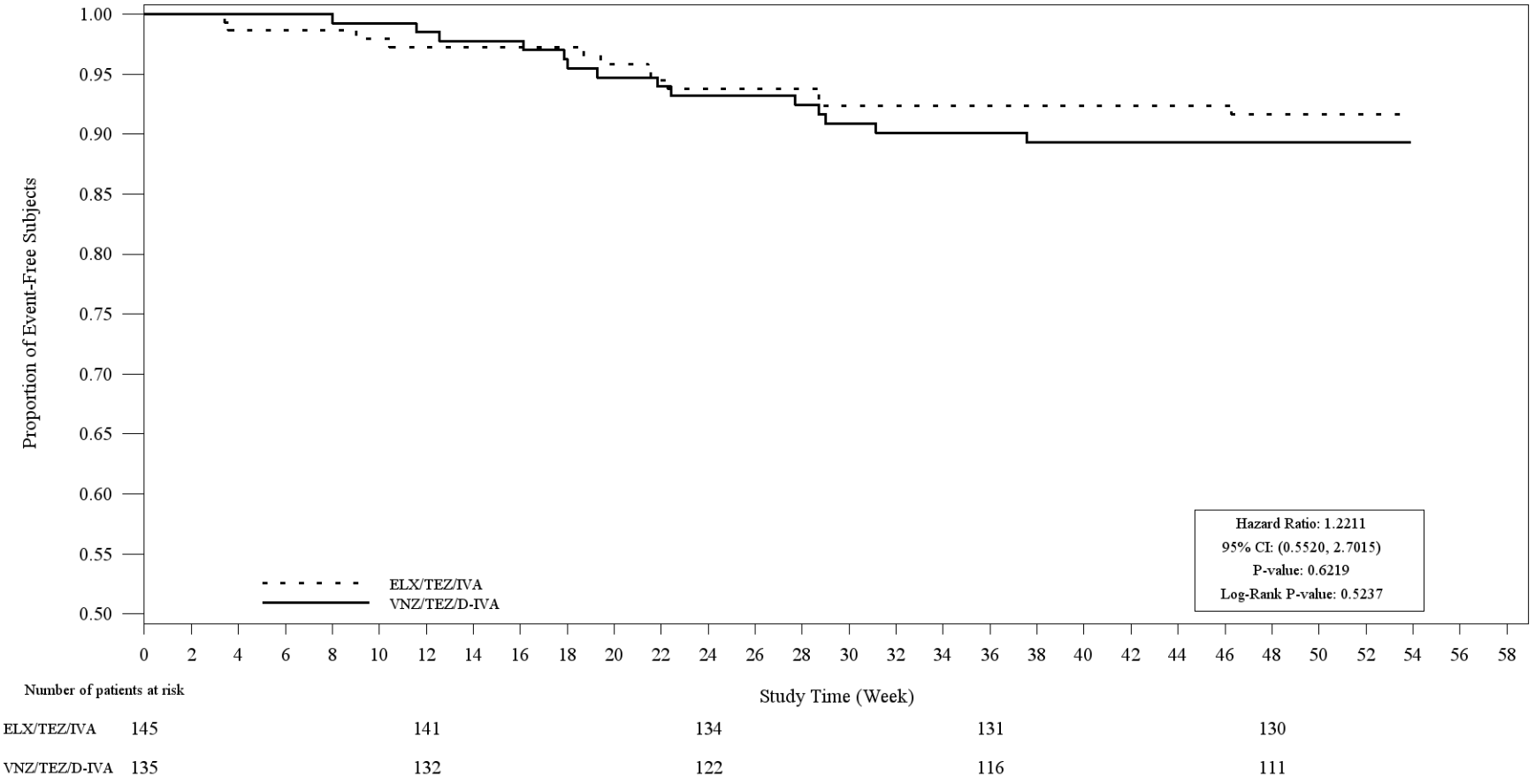
ELX/TEZ/IVA	144	141	139	138	136
VNZ/TEZ/D-IVA	149	144	142	140	139

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-iv-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Female



Number of patients at risk

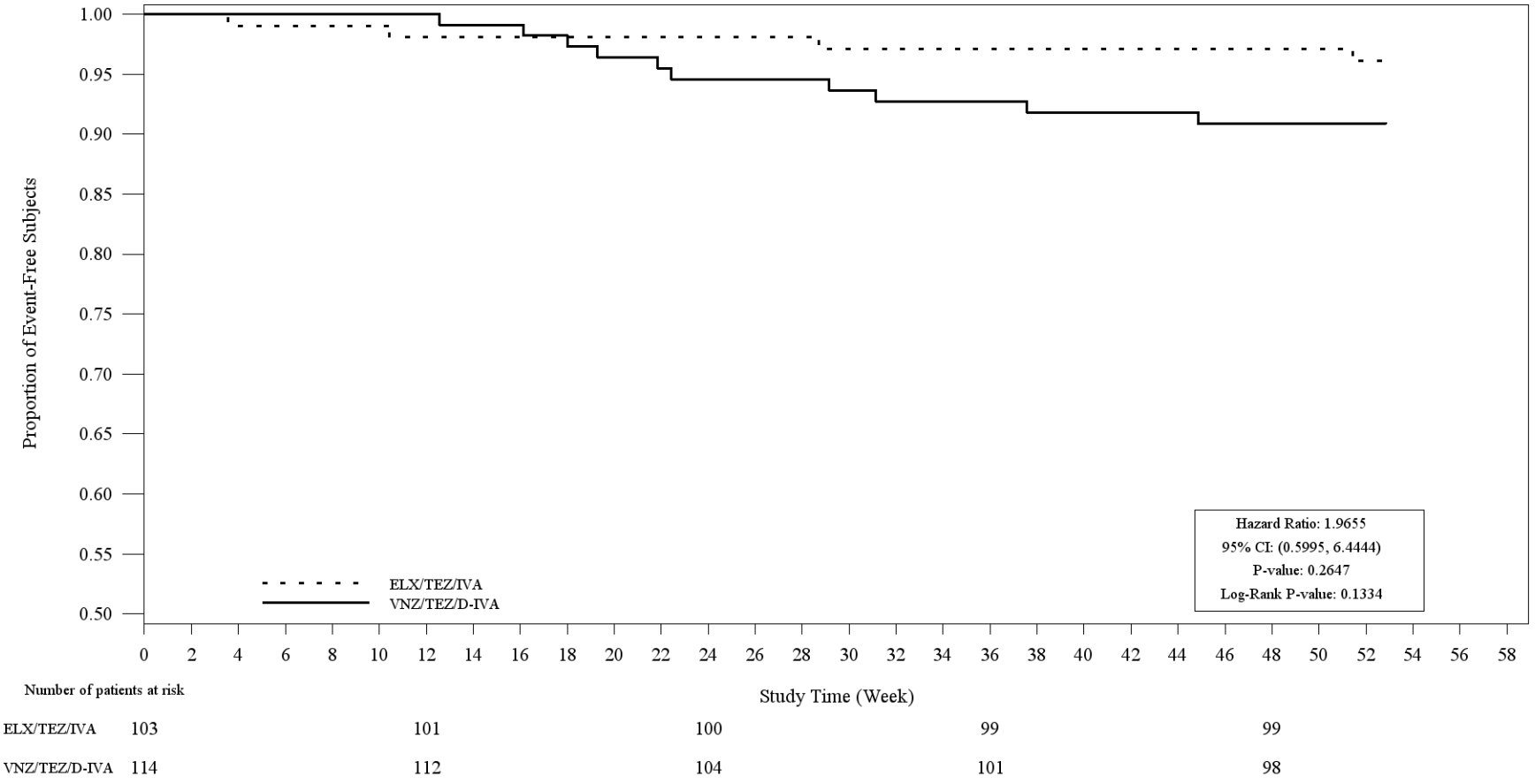
ELX/TEZ/IVA	145	141	134	131	130
VNZ/TEZ/D-IVA	135	132	122	116	111

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-iv-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = North America



Number of patients at risk

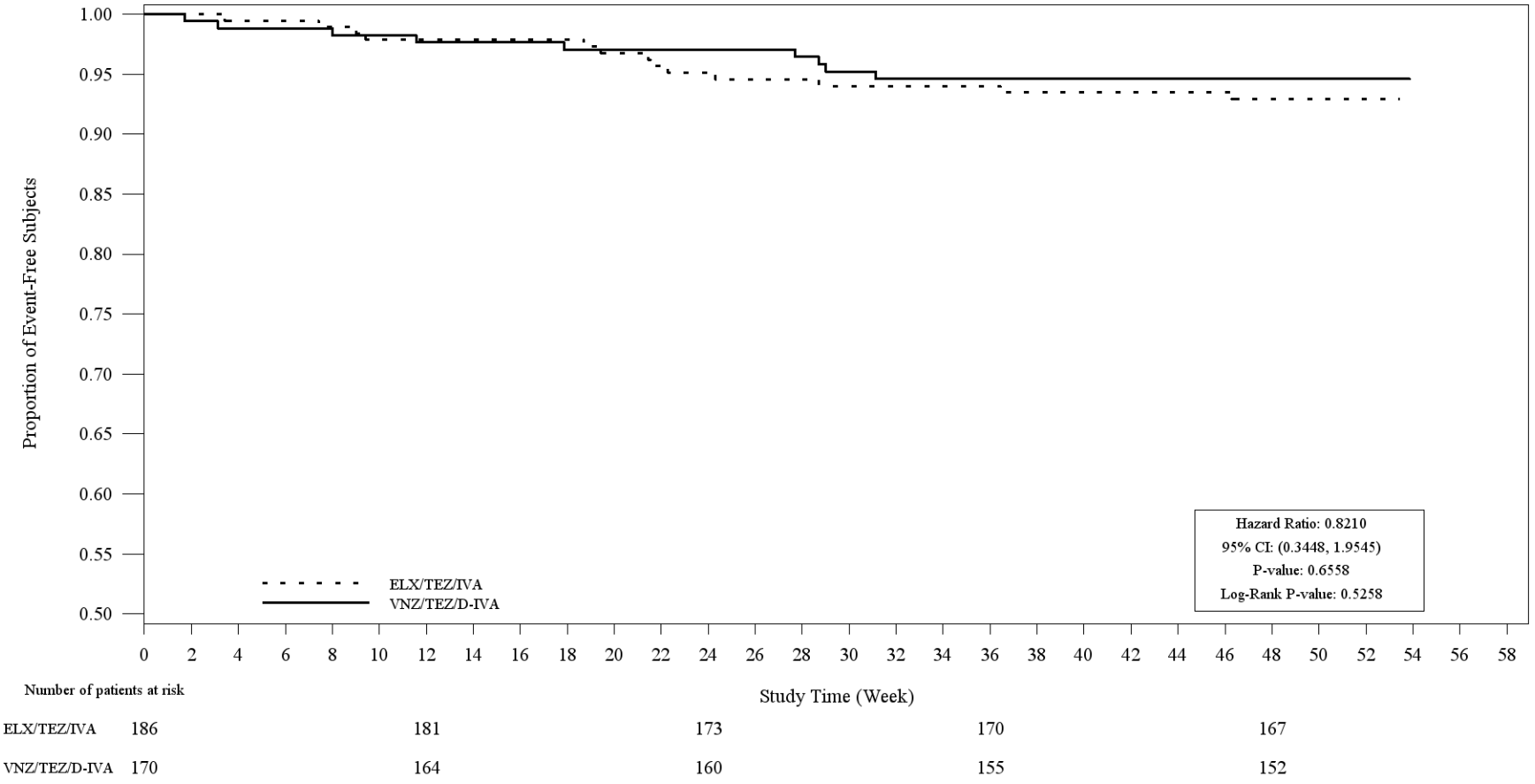
ELX/TEZ/IVA	103	101	100	99	99
VNZ/TEZ/D-IVA	114	112	104	101	98

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-iv-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = Rest of the World



Number of patients at risk

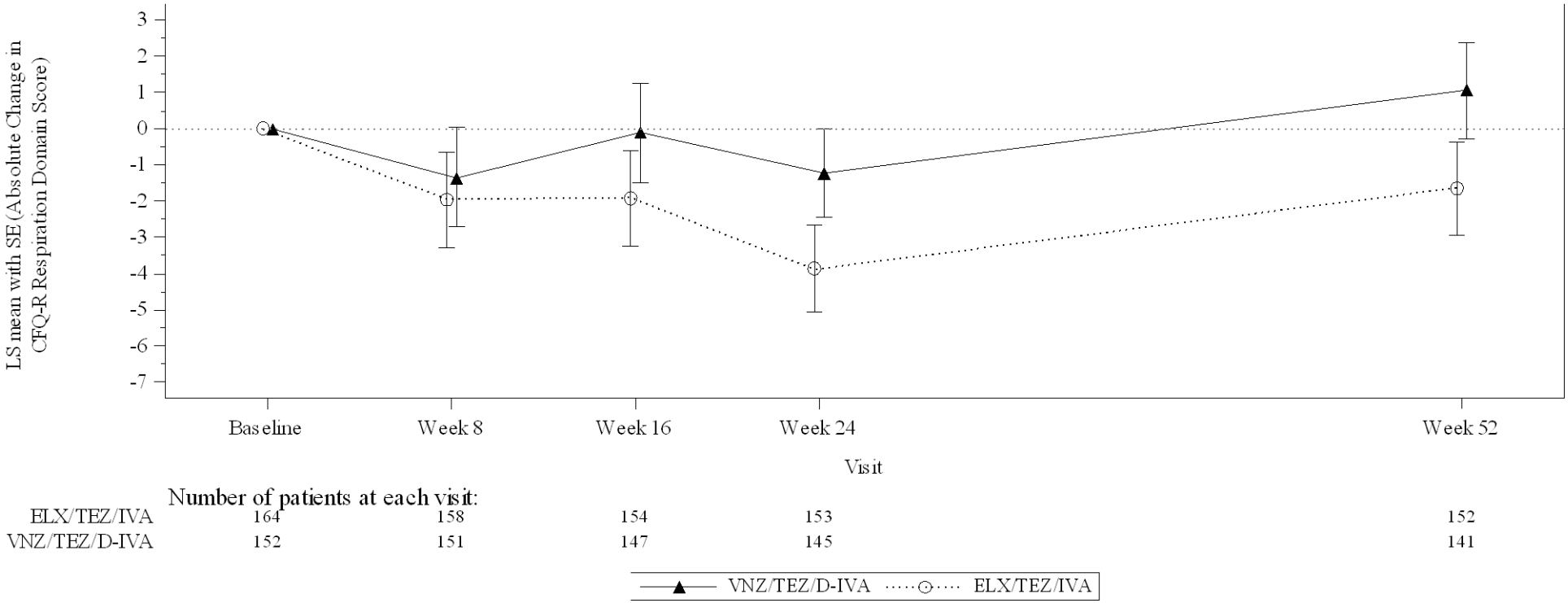
ELX/TEZ/IVA	186	181	173	170	167
VNZ/TEZ/D-IVA	170	164	160	155	152

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-ce-pe-iv-km-52wks-sub-103.sas Creation: 04MAR2025 16:02

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
ppFEV$_1$ at baseline <70 %

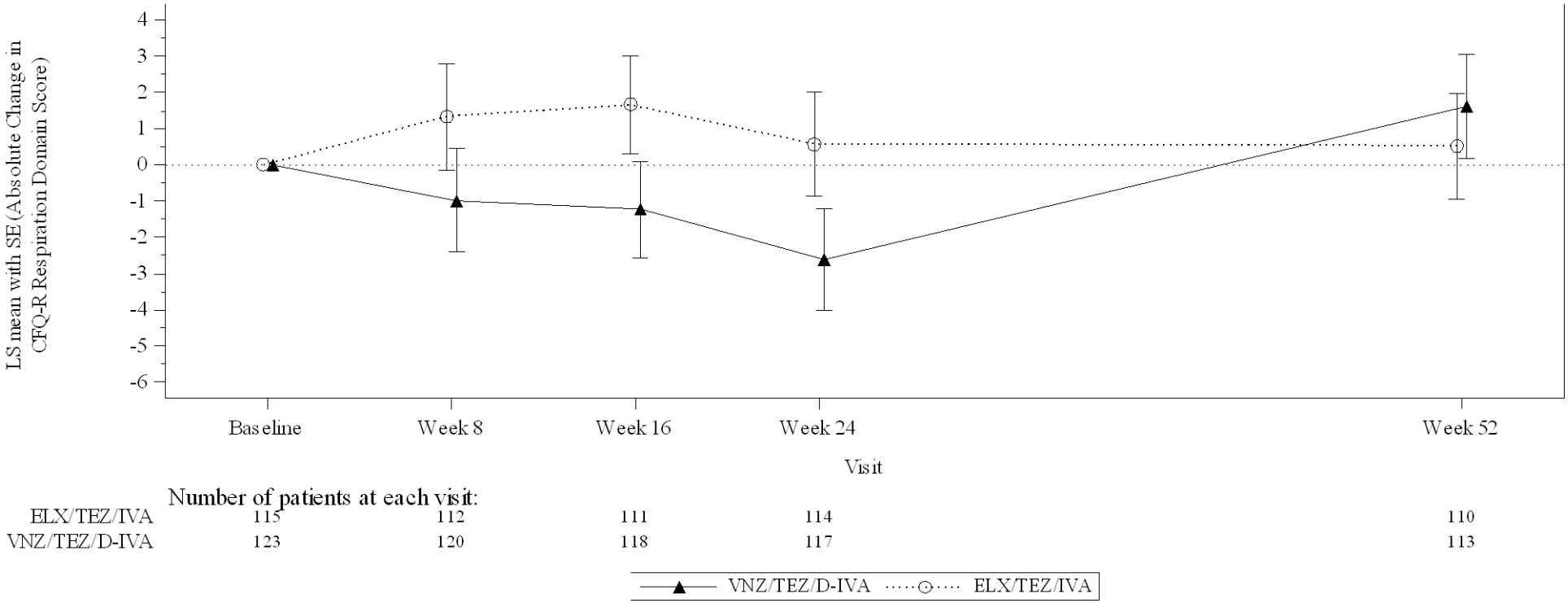


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
ppFEV$_1$ at baseline ≥70 %

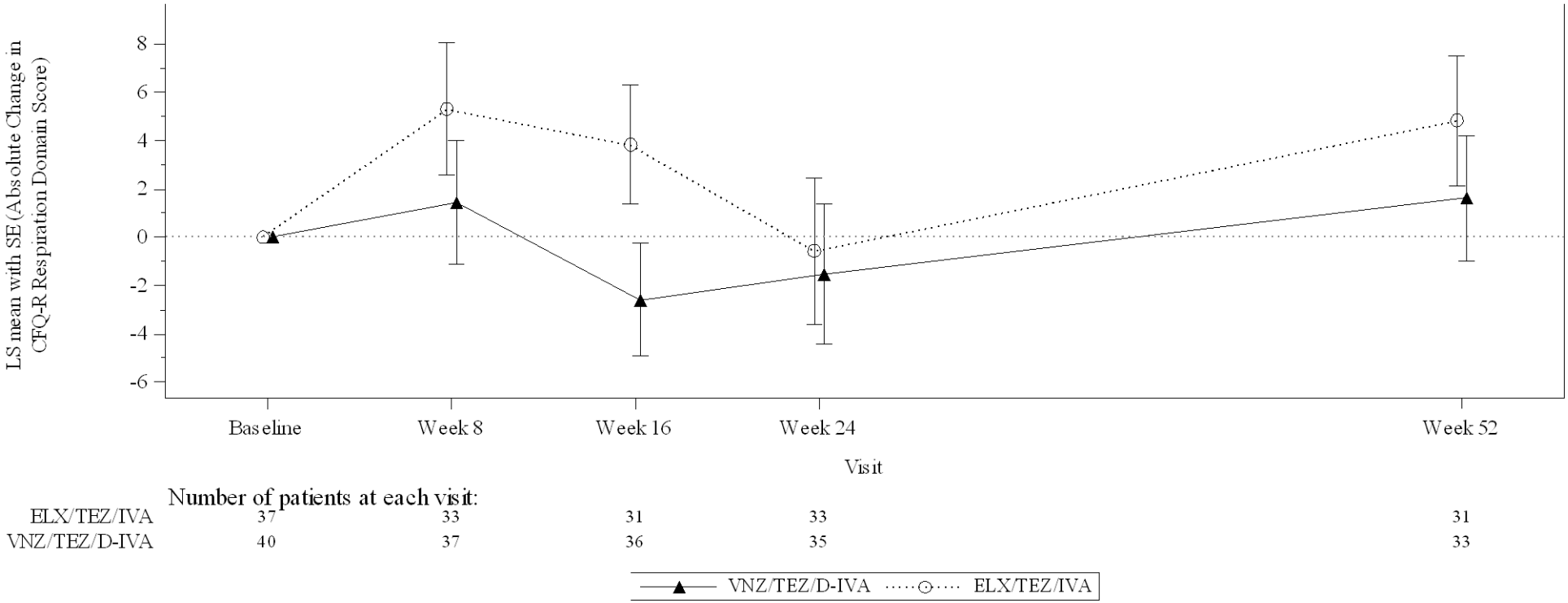


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Age at screening <18 years

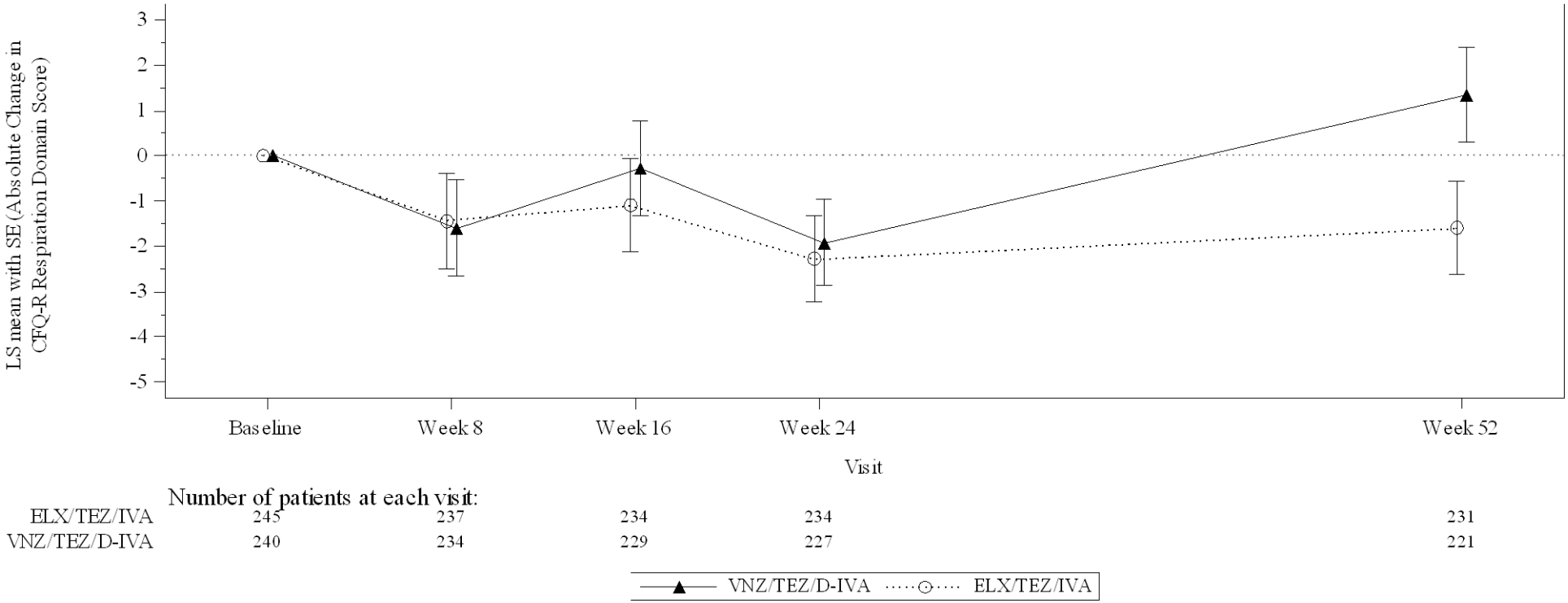


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Age at screening ≥18 years

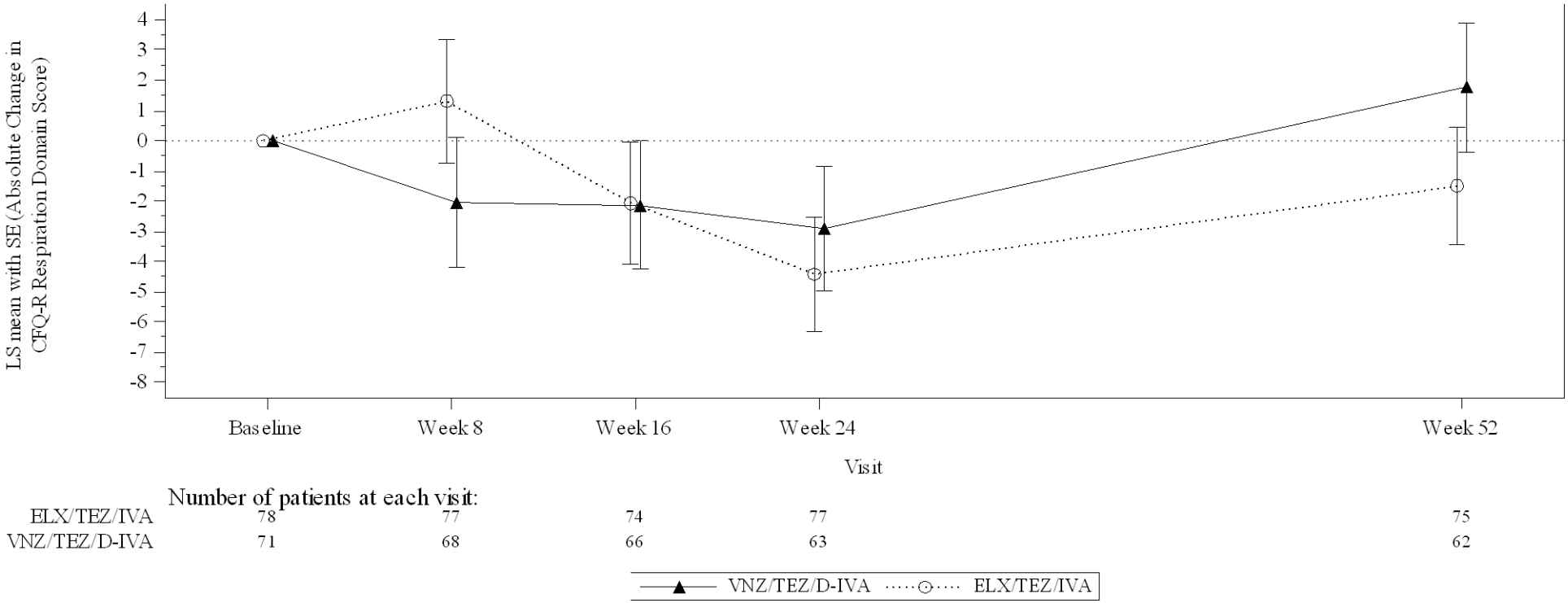


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
SwCl at baseline <30 mmol/L



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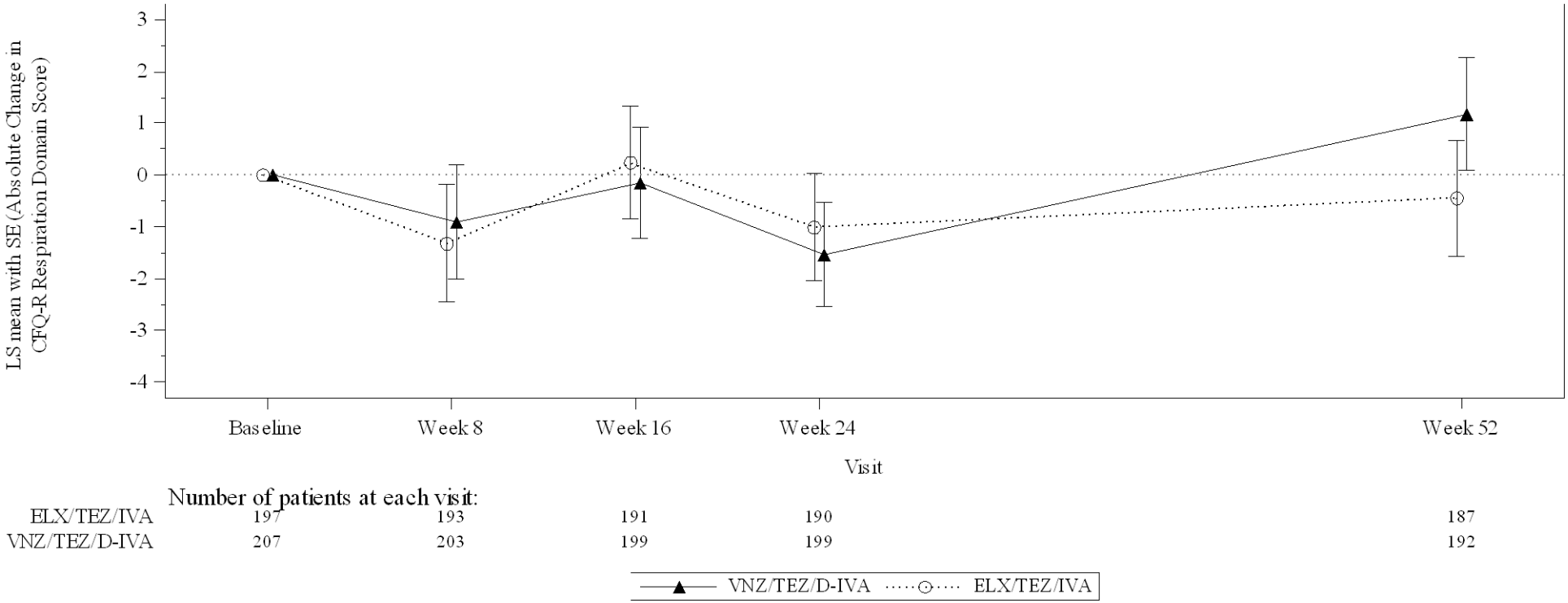
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
SwCl at baseline ≥30 mmol/L



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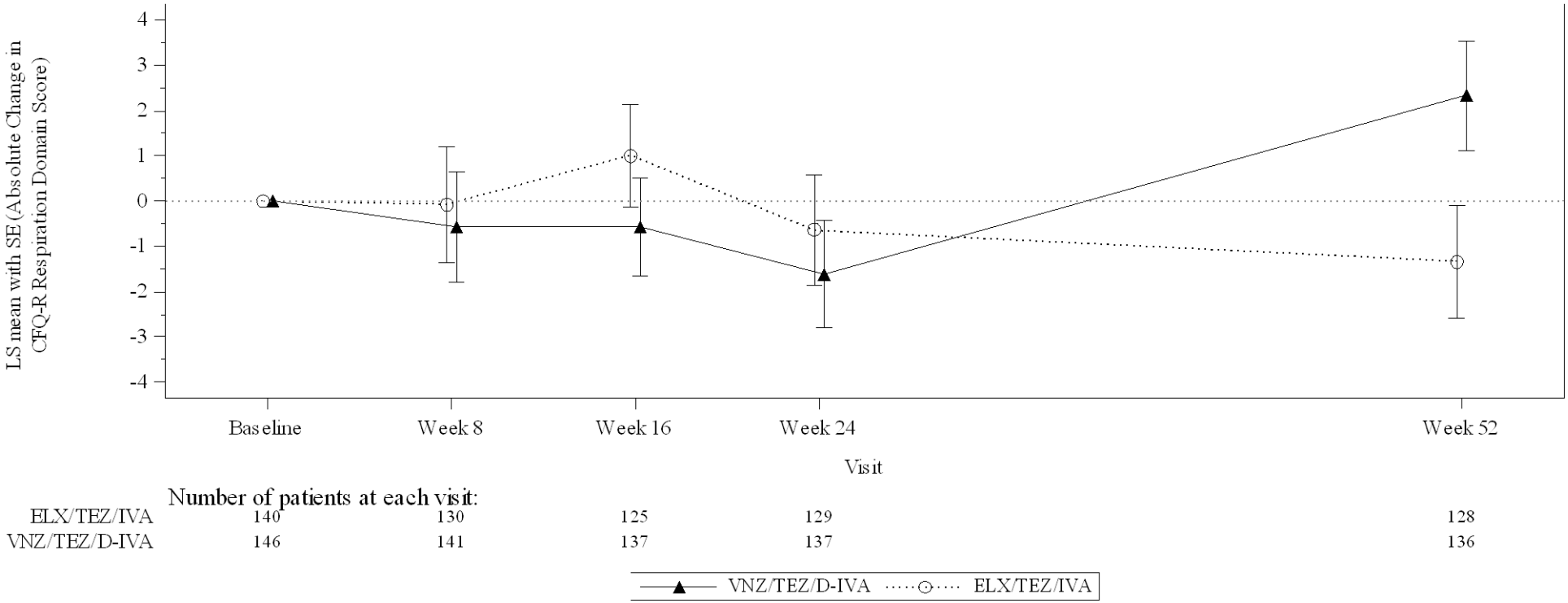
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Sex = Male



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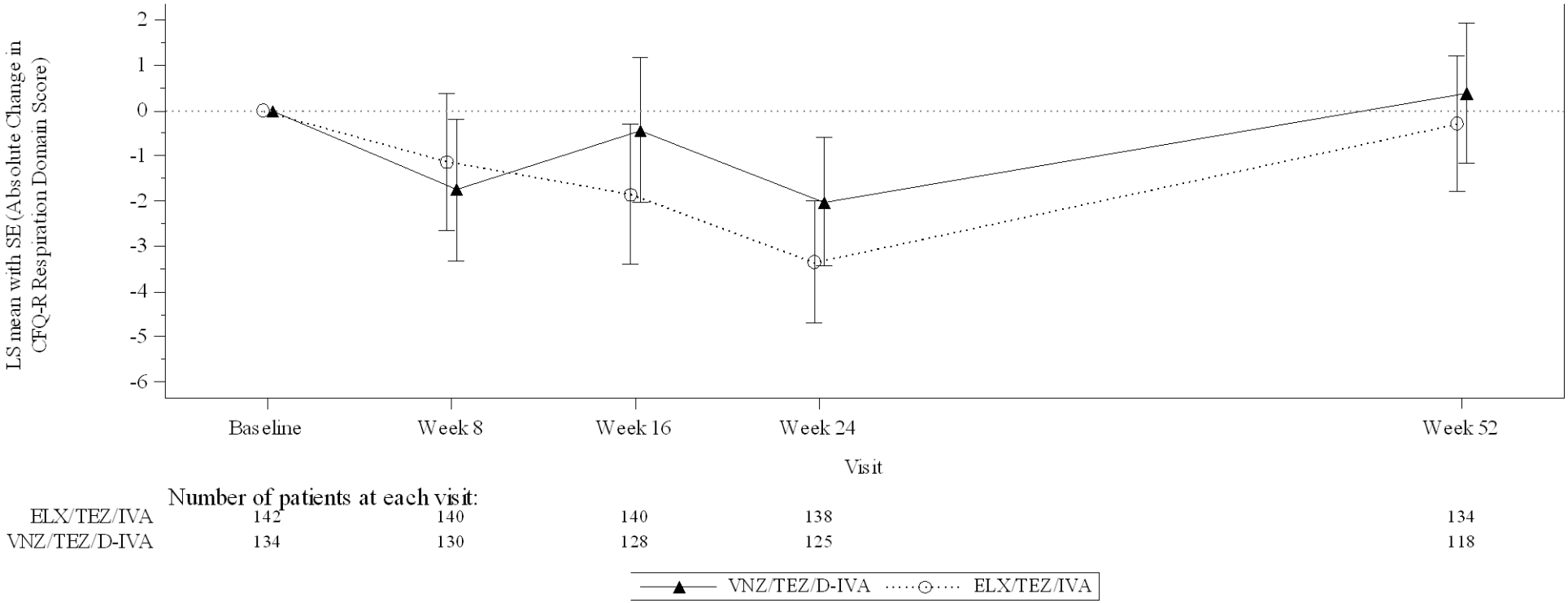
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Sex = Female



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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Region = North America

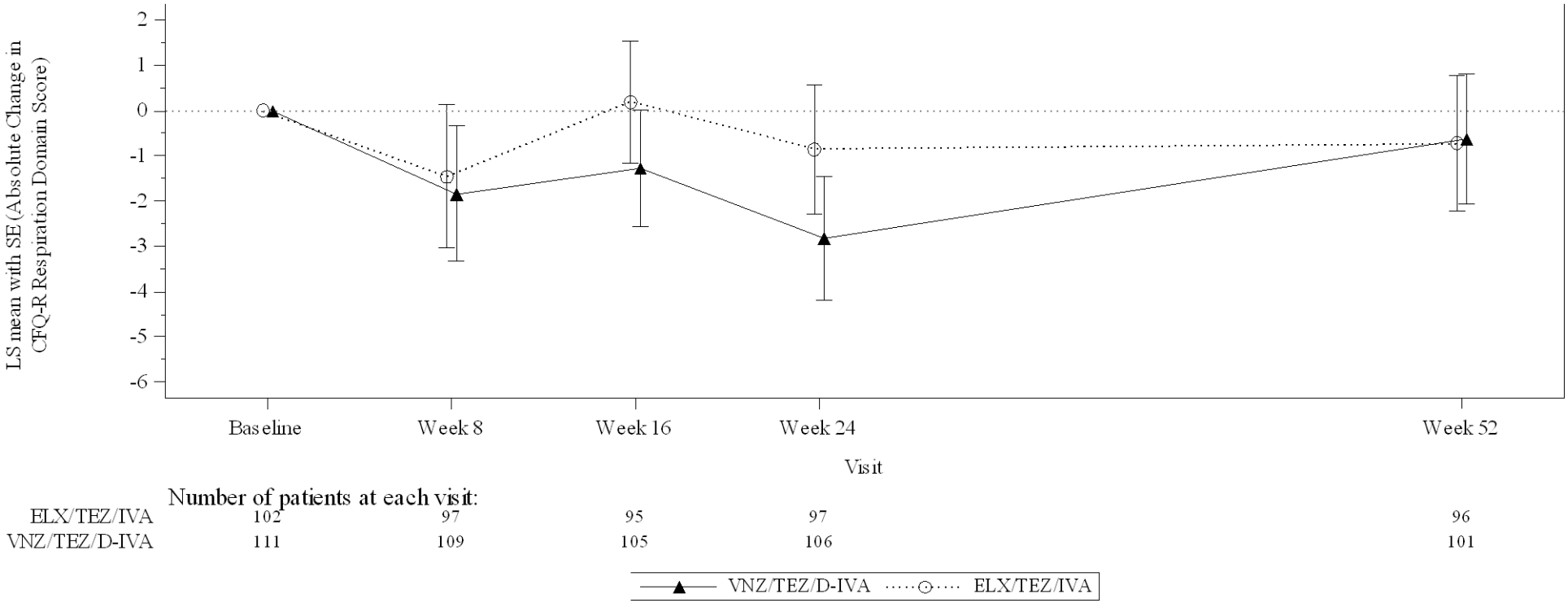

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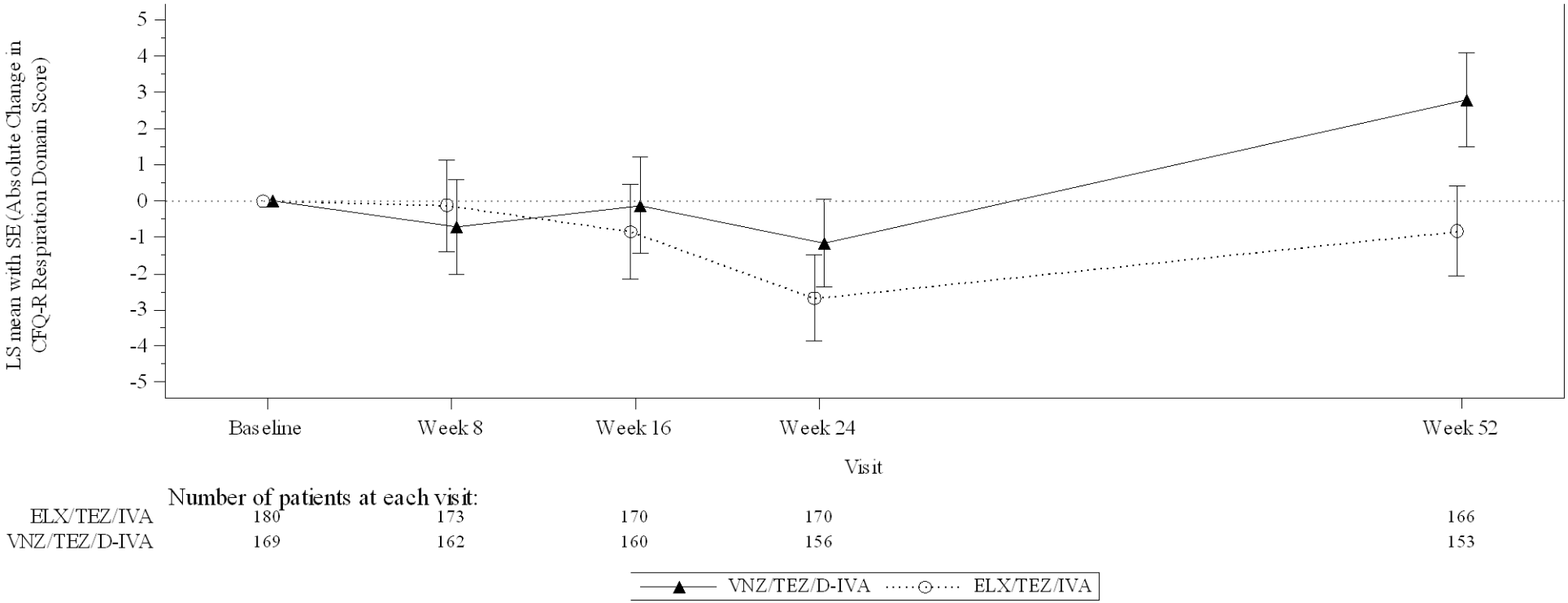
Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Region = Rest of World



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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
ppFEV$_1$ at baseline <70 %

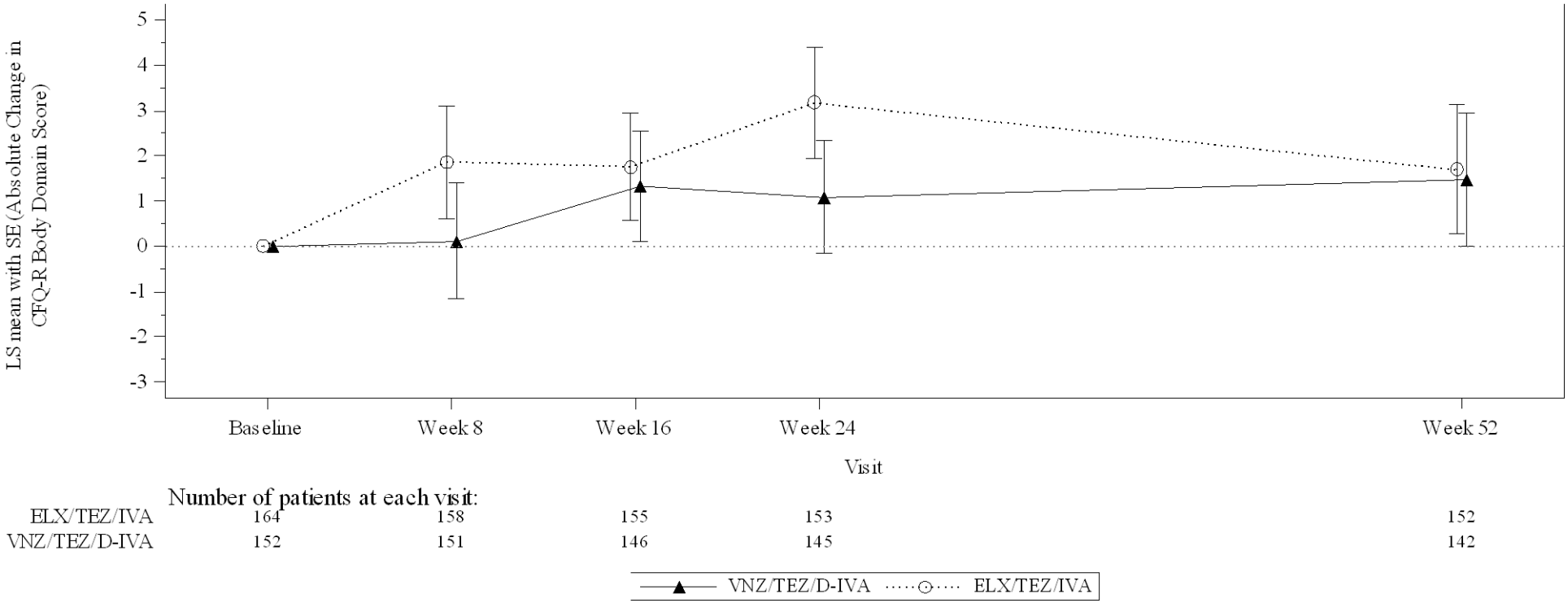

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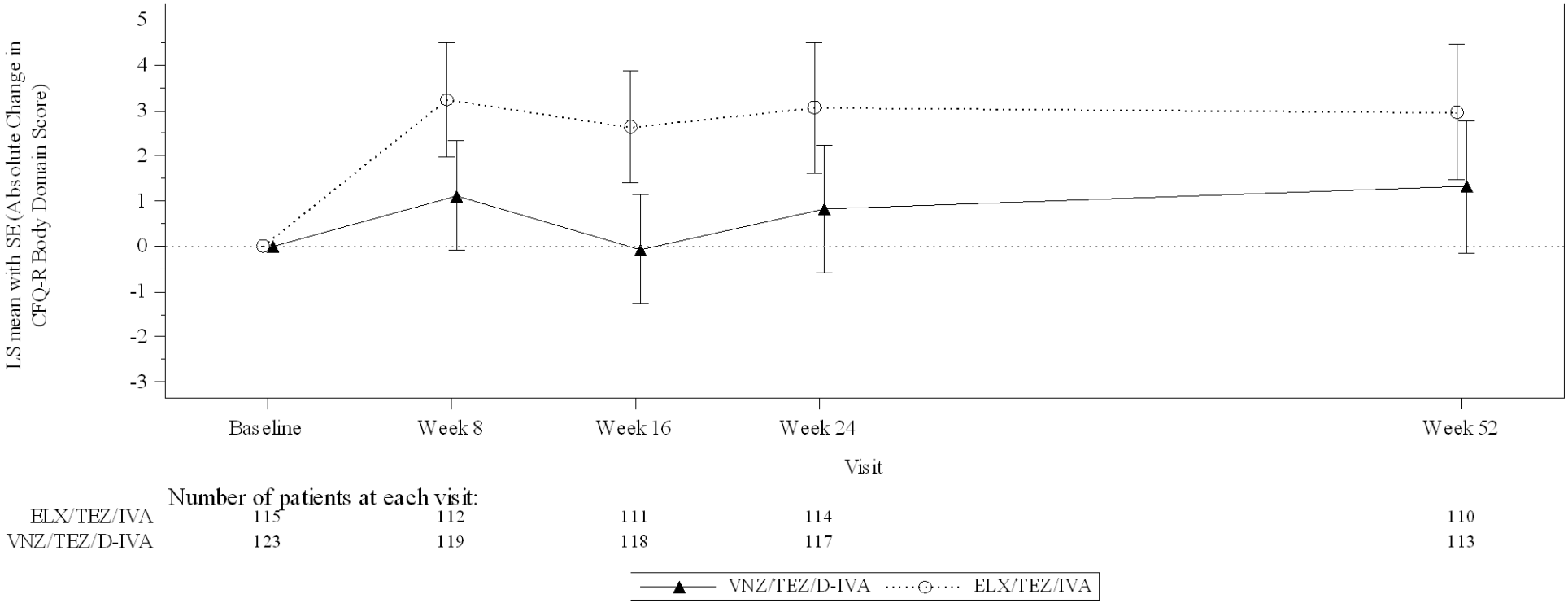
Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
ppFEV$_1$ at baseline ≥70 %



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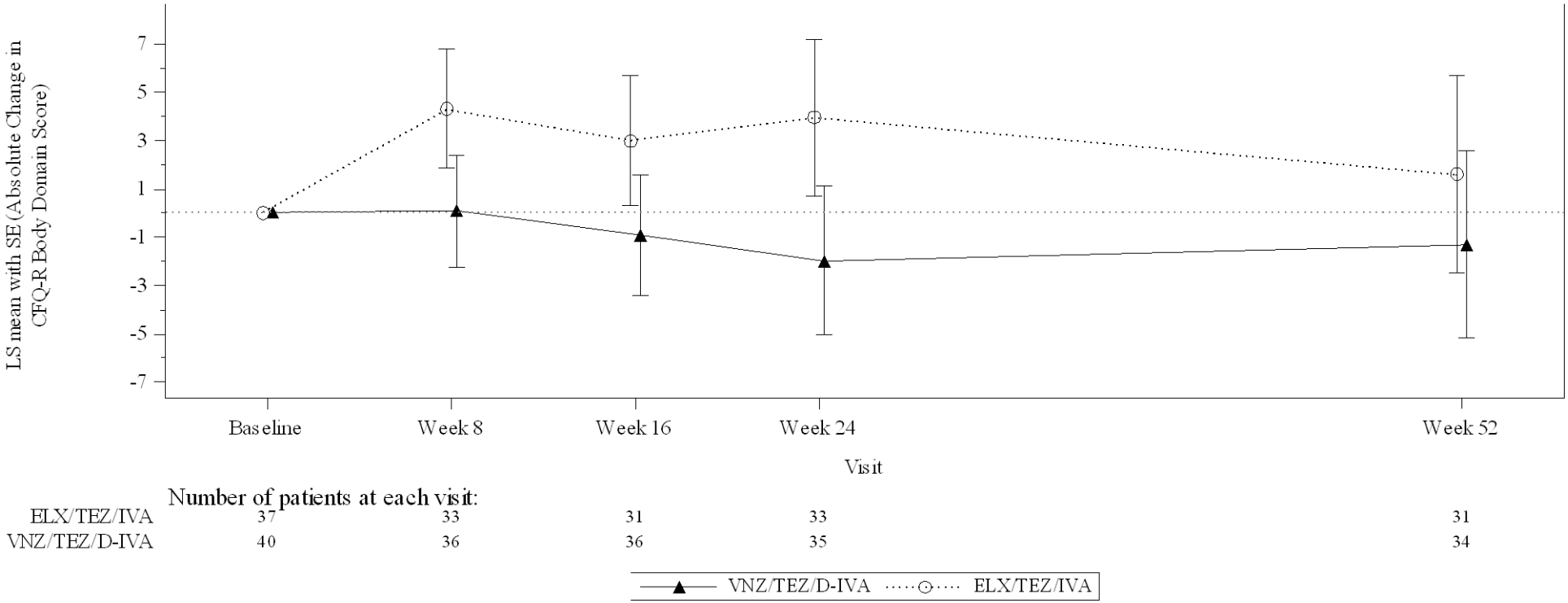
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years



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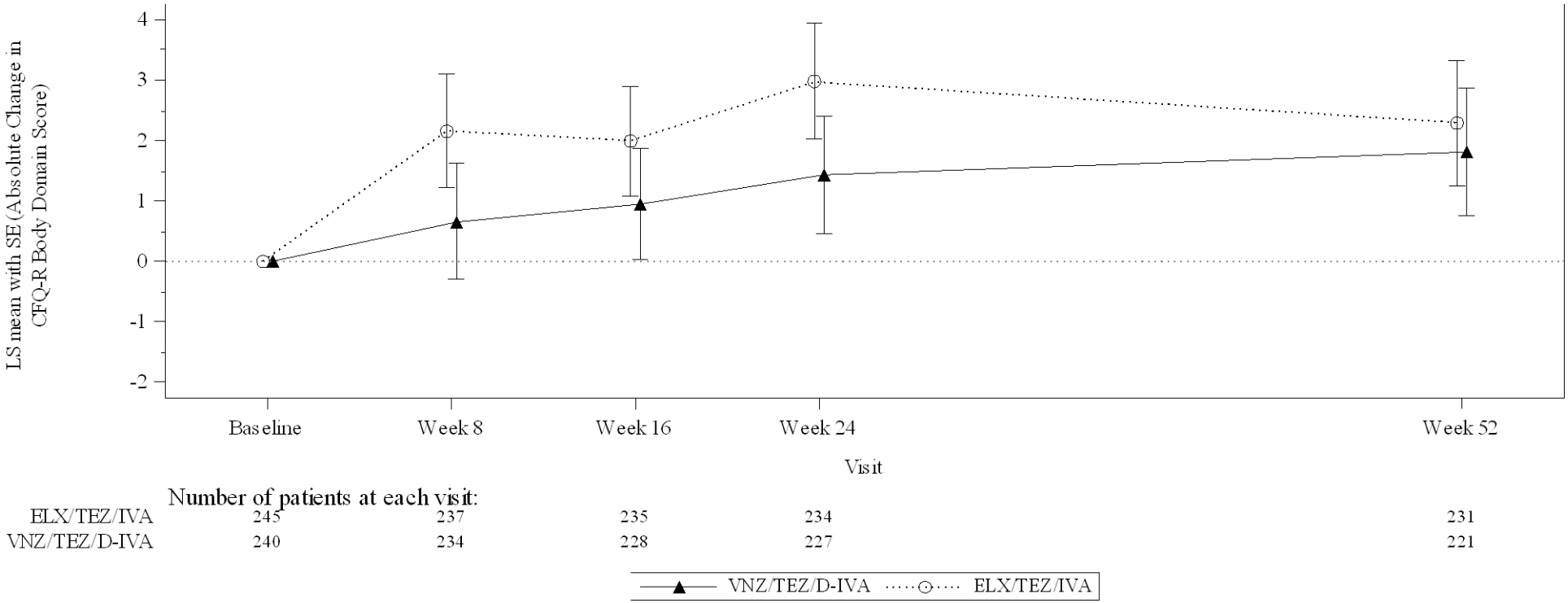
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years



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Full Analysis Set

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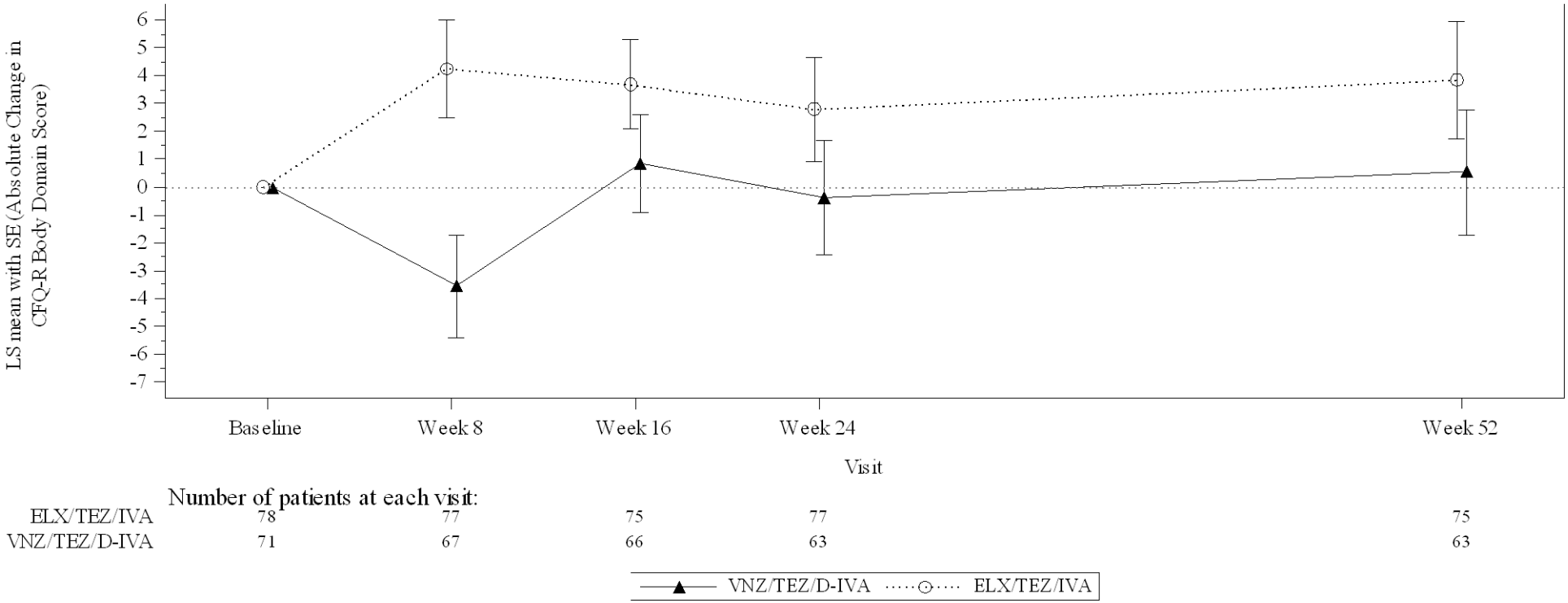
Domain: Body
SwCl at baseline <30 mmol/L



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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

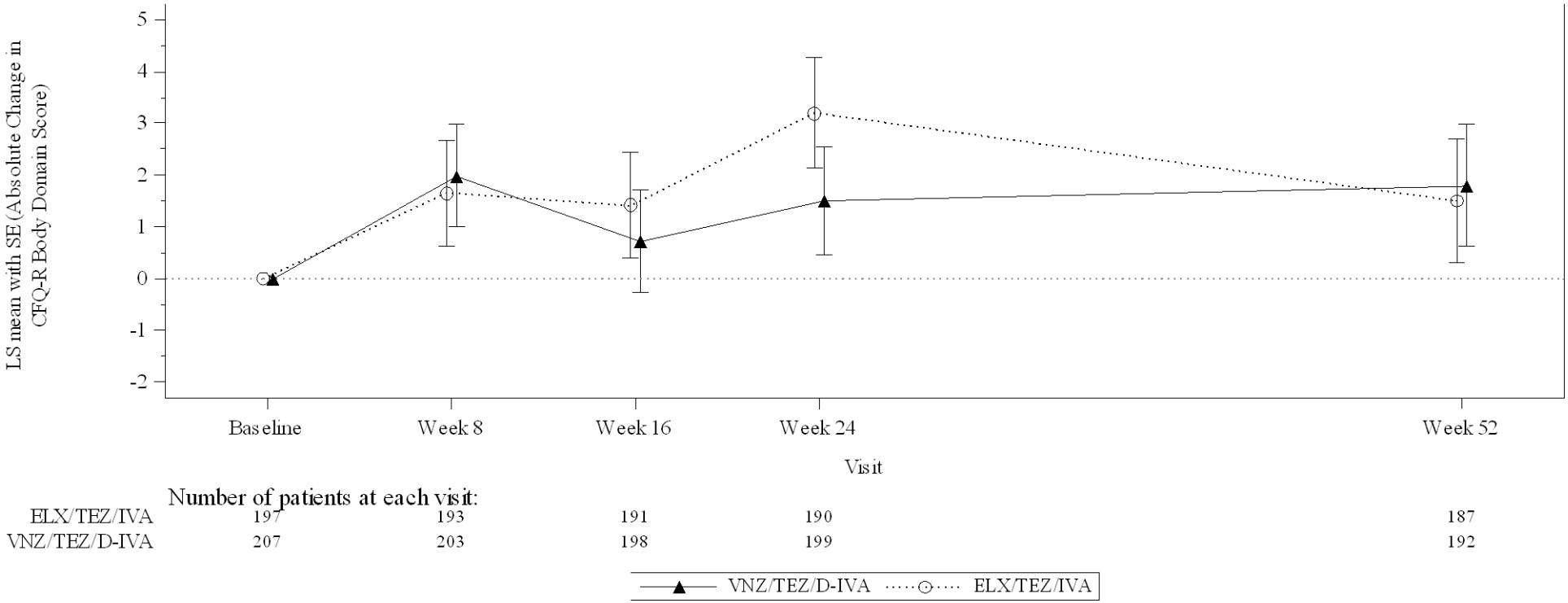

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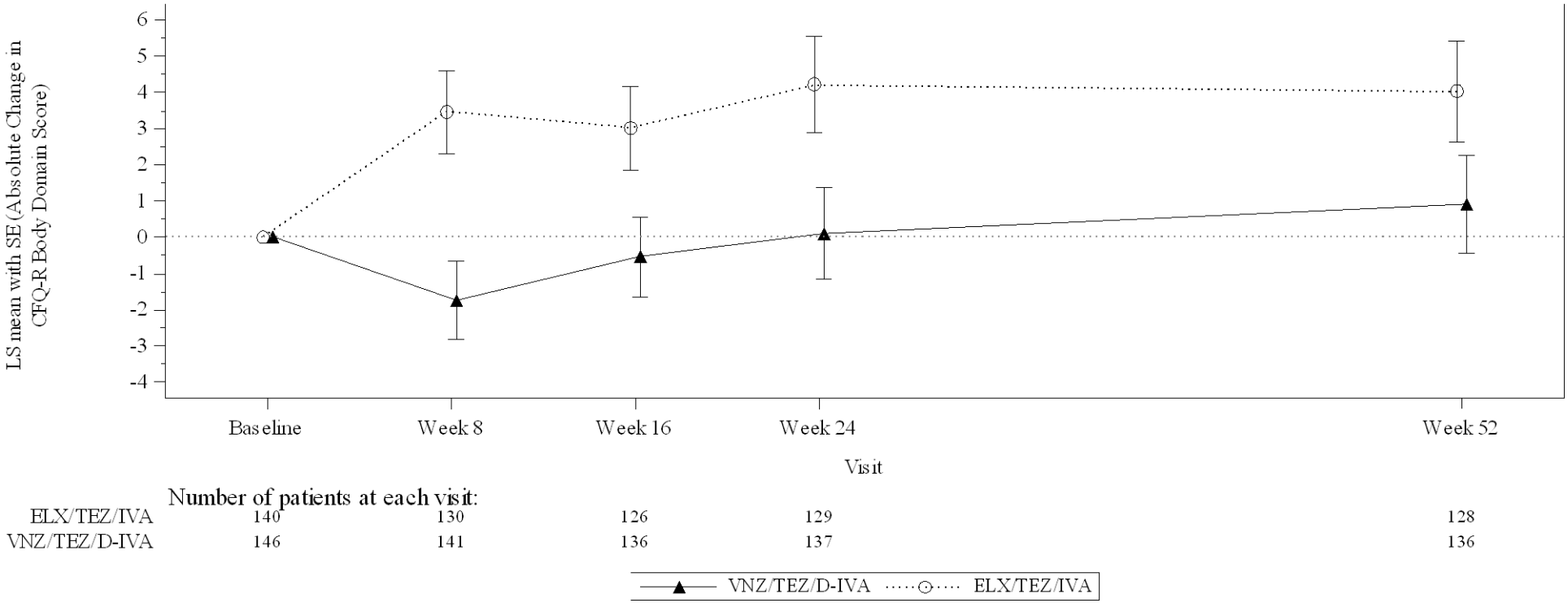
Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male



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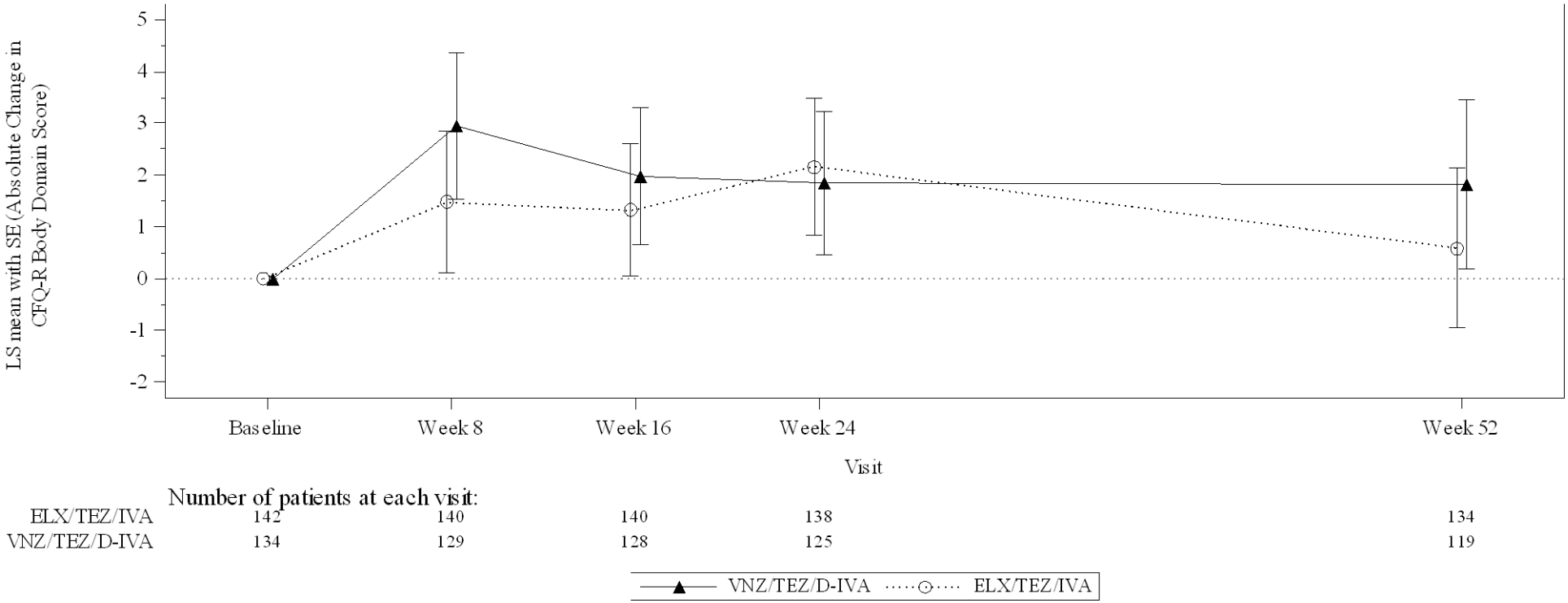
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female



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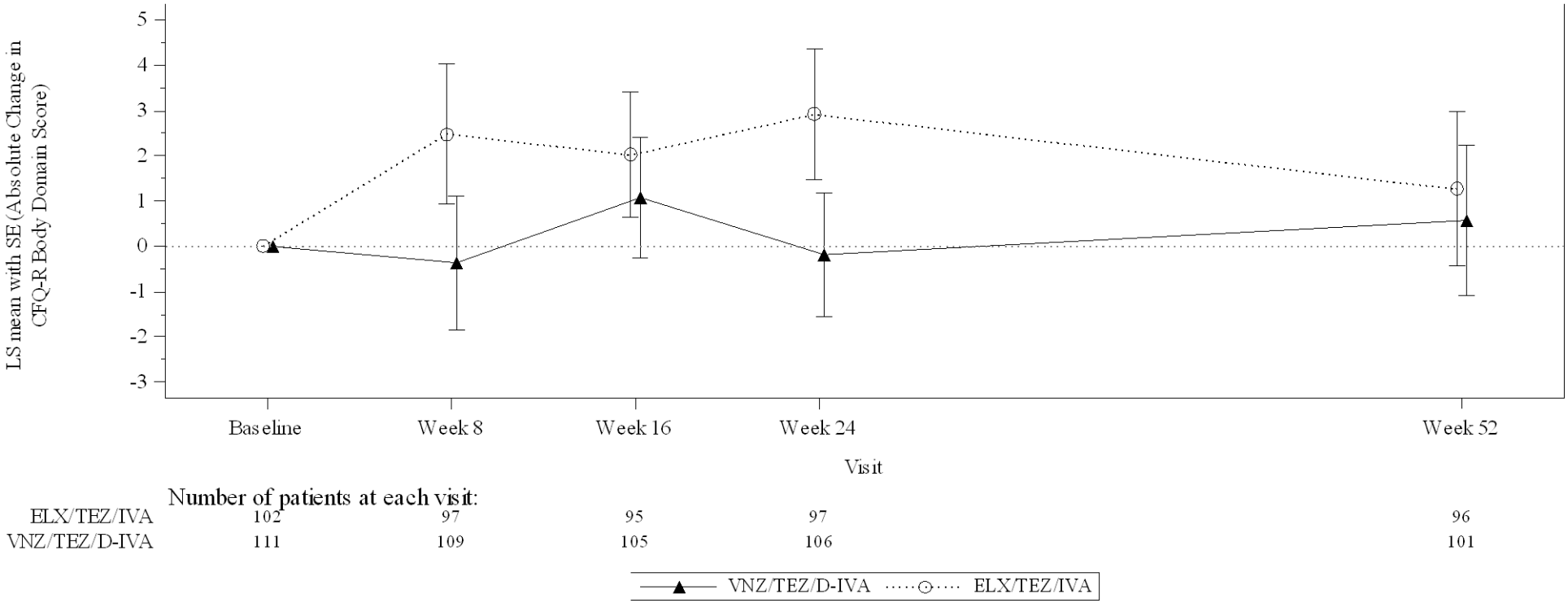
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America



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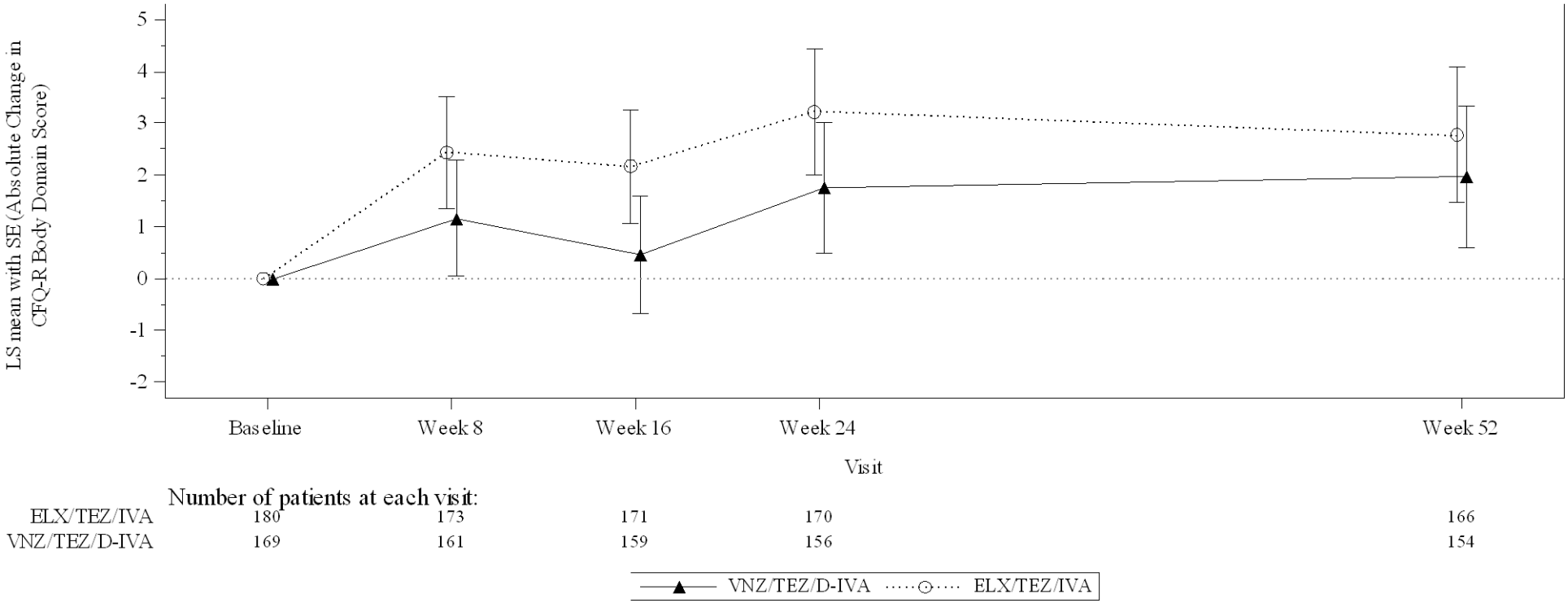
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World



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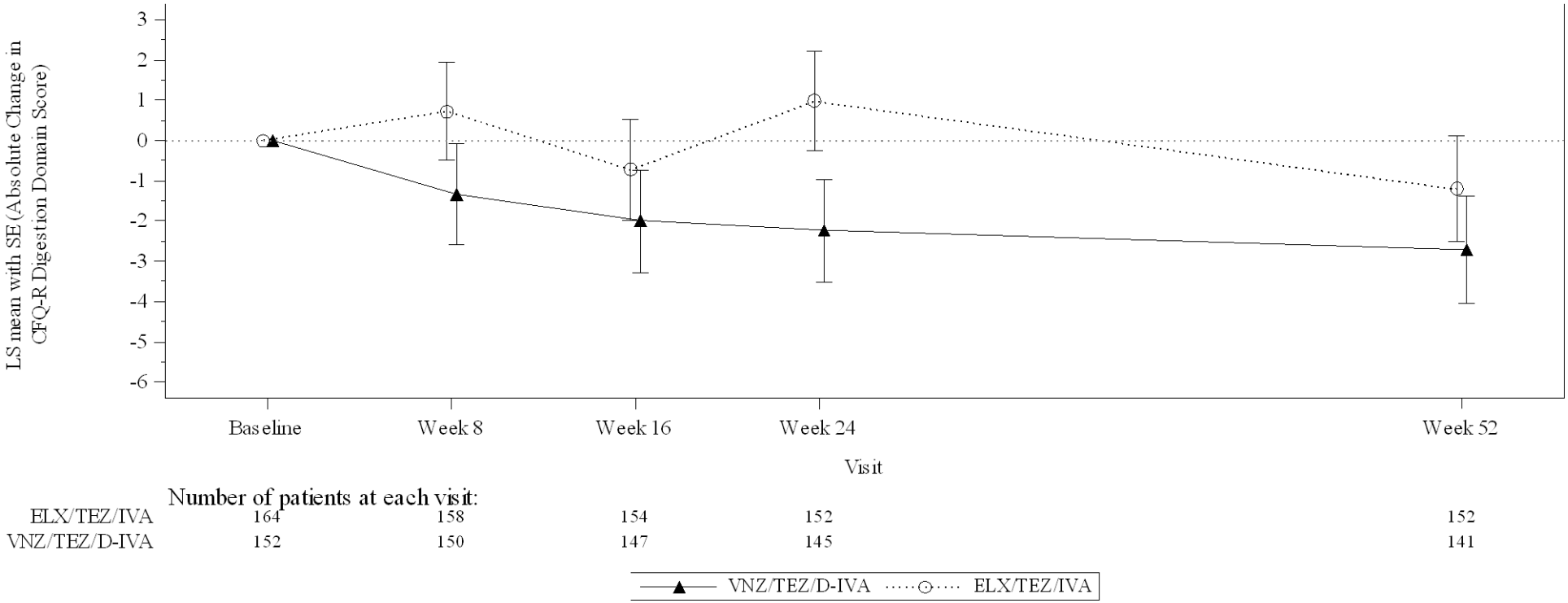
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
ppFEV$_1$ at baseline <70 %



Number of patients at each visit:

ELX/TEZ/IVA	164	158	154	152	152
VNZ/TEZ/D-IVA	152	150	147	145	141

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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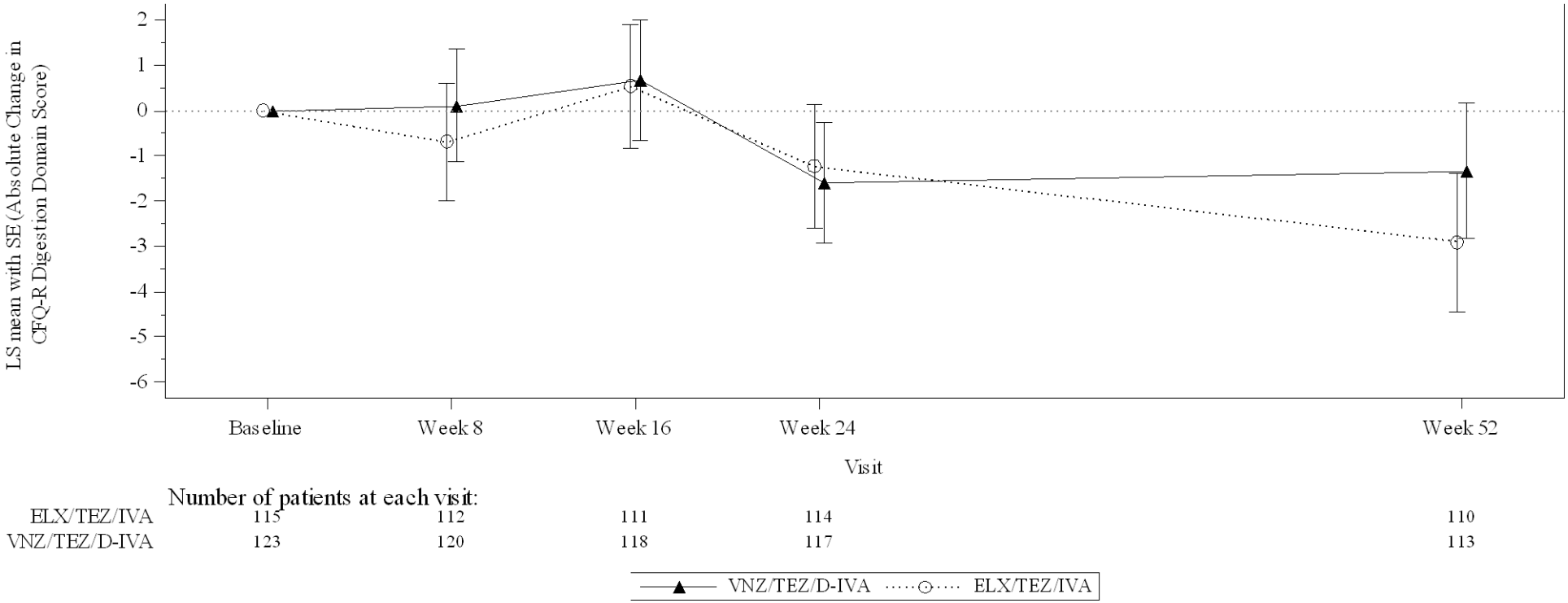
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
ppFEV$_1$ at baseline ≥70 %



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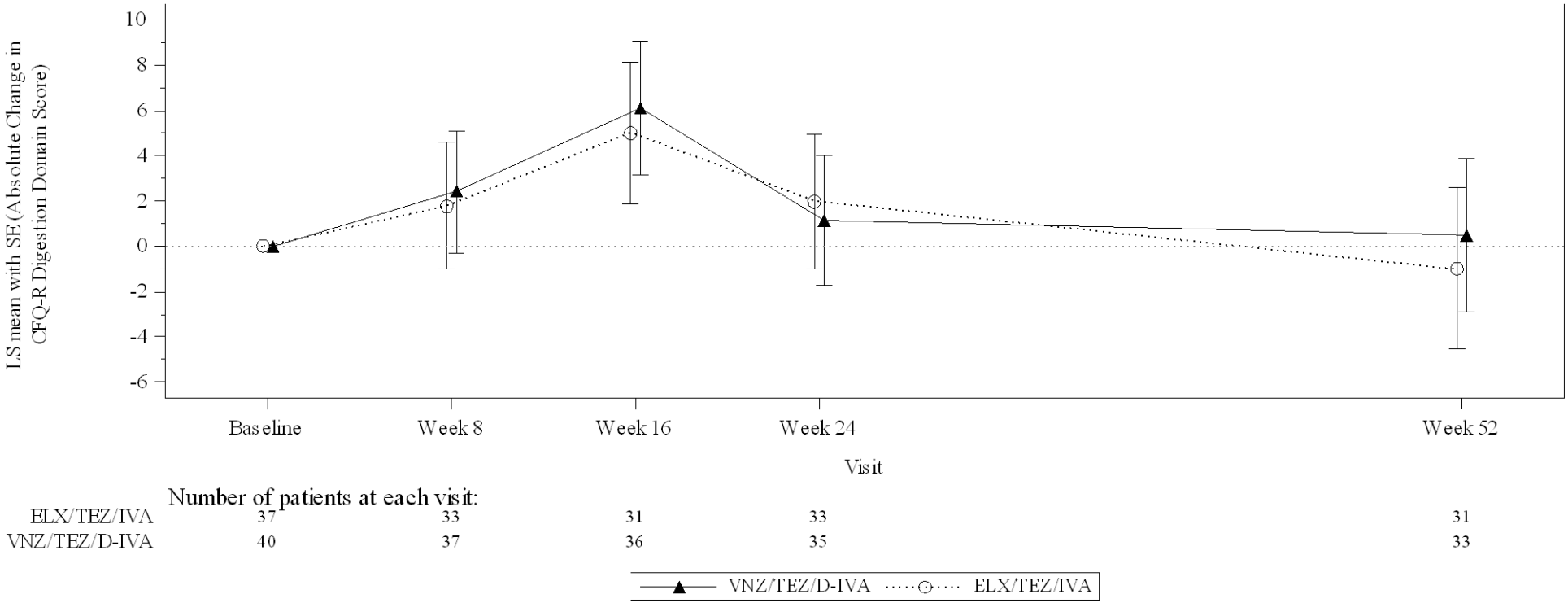
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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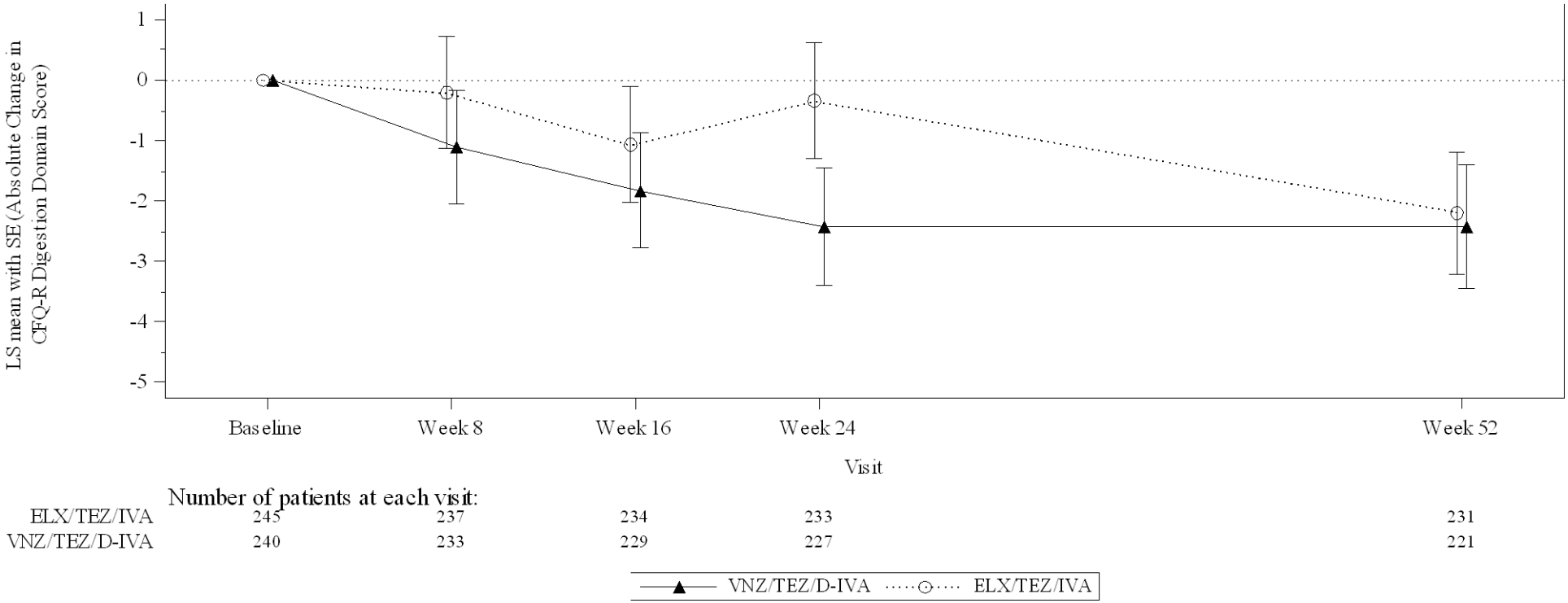
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years



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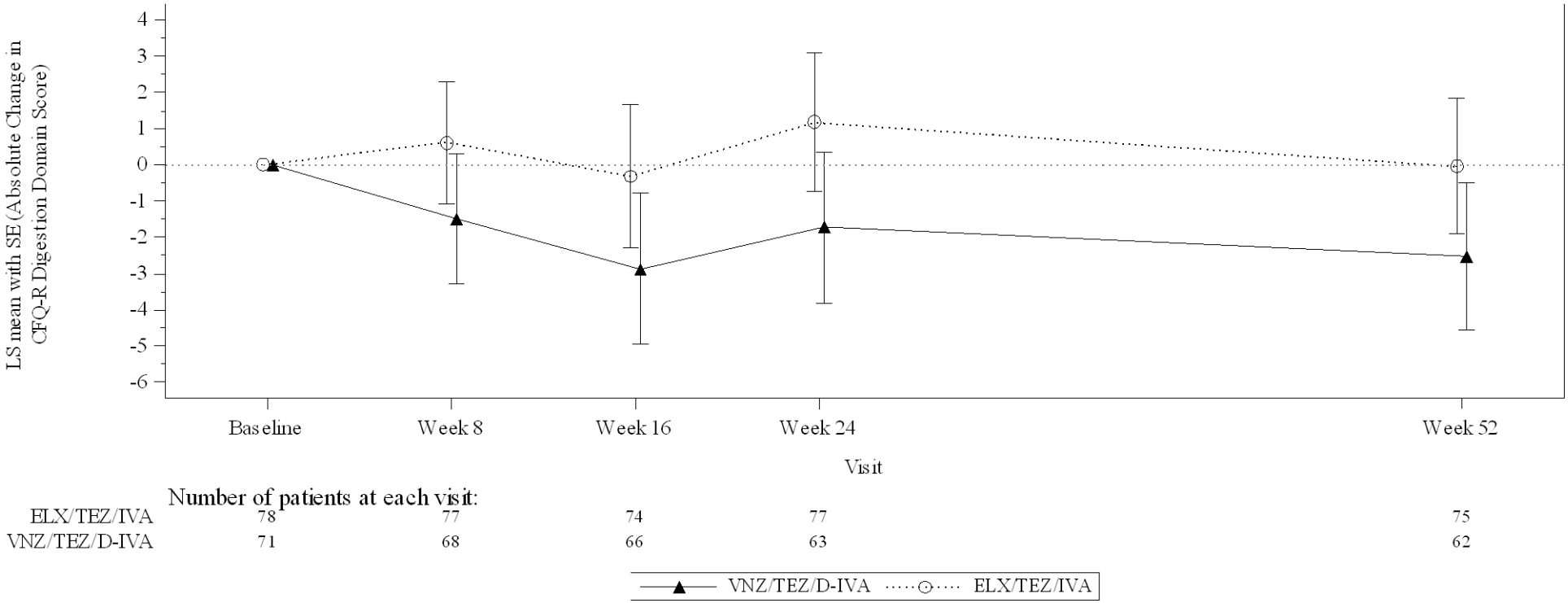
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L



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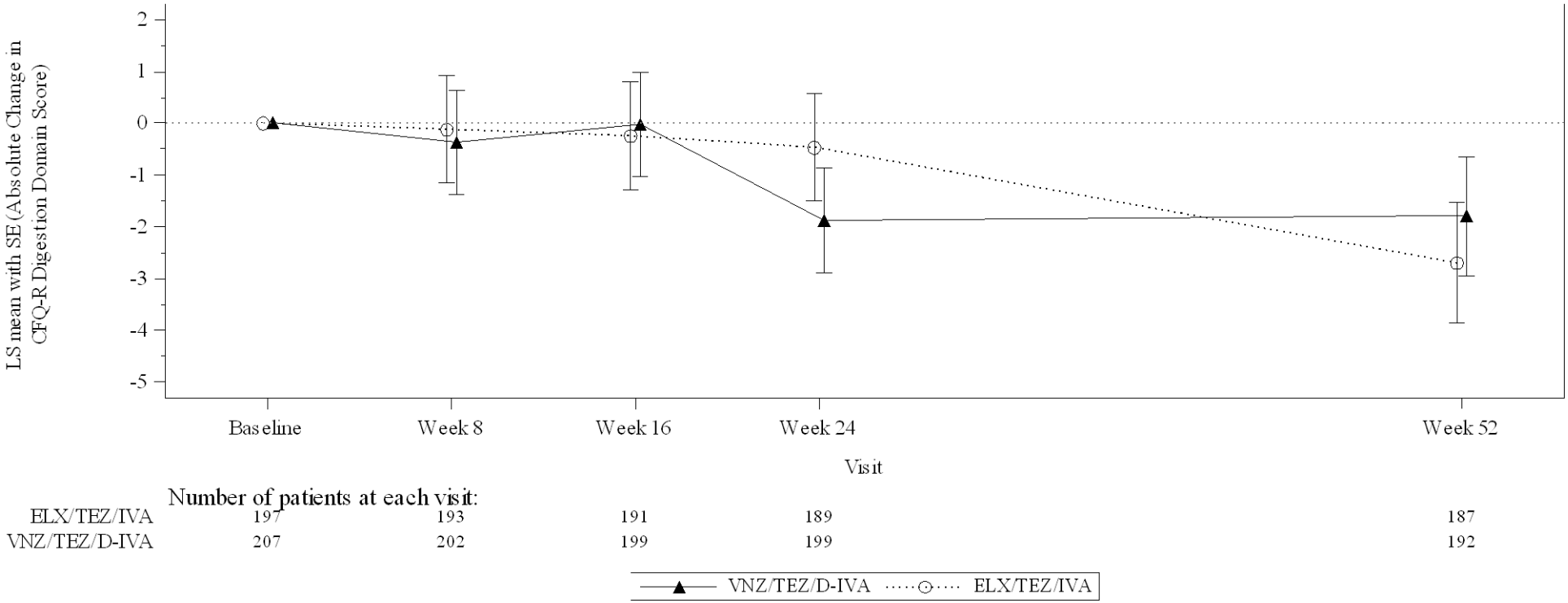
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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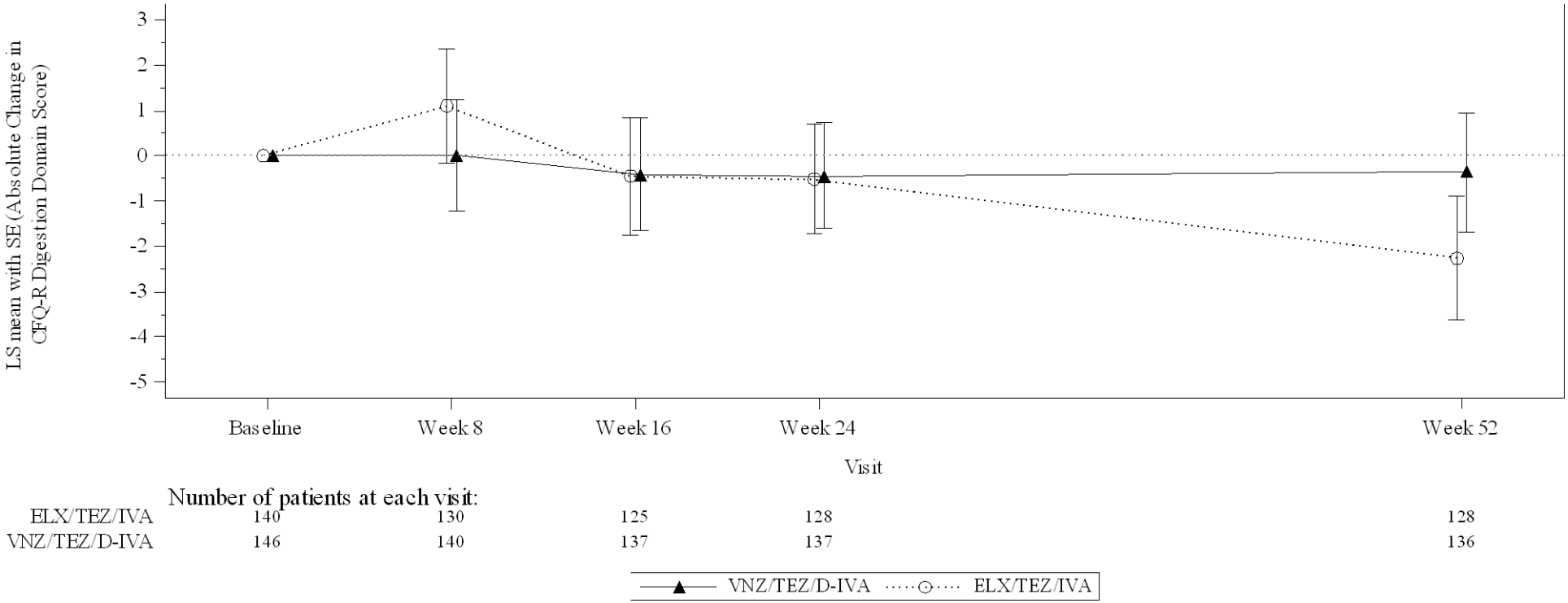
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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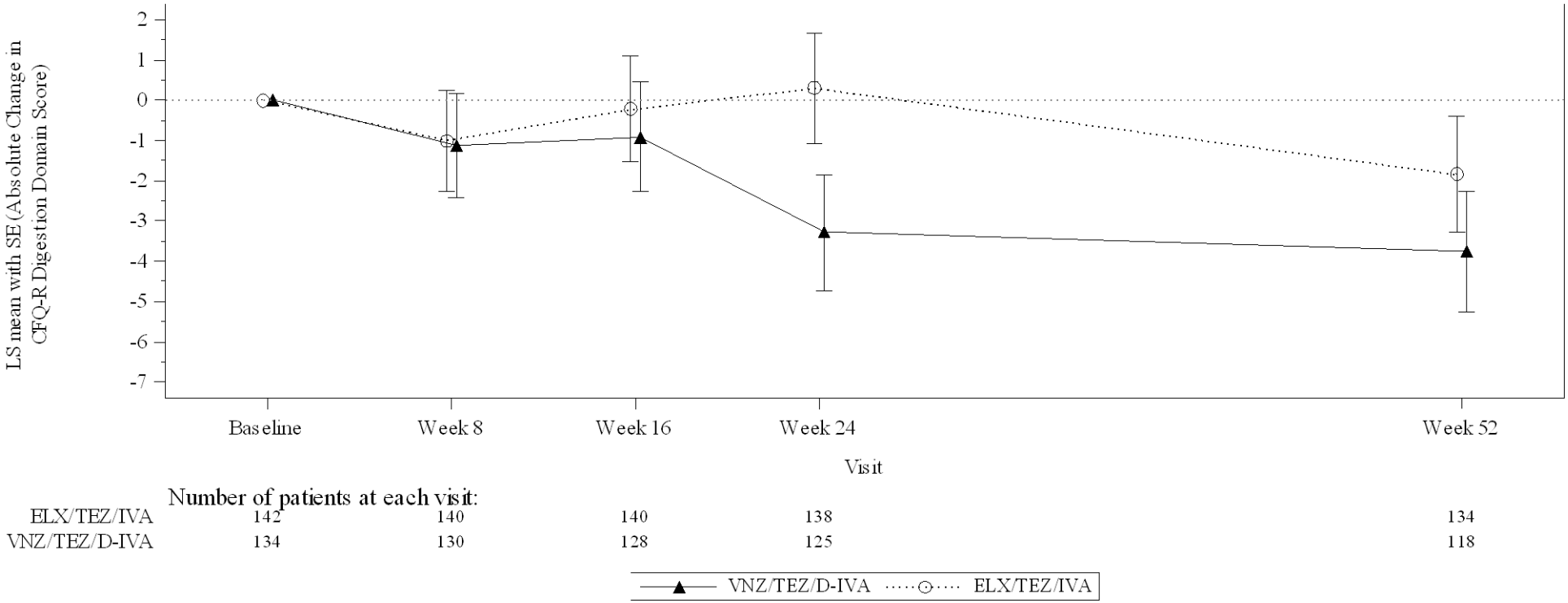
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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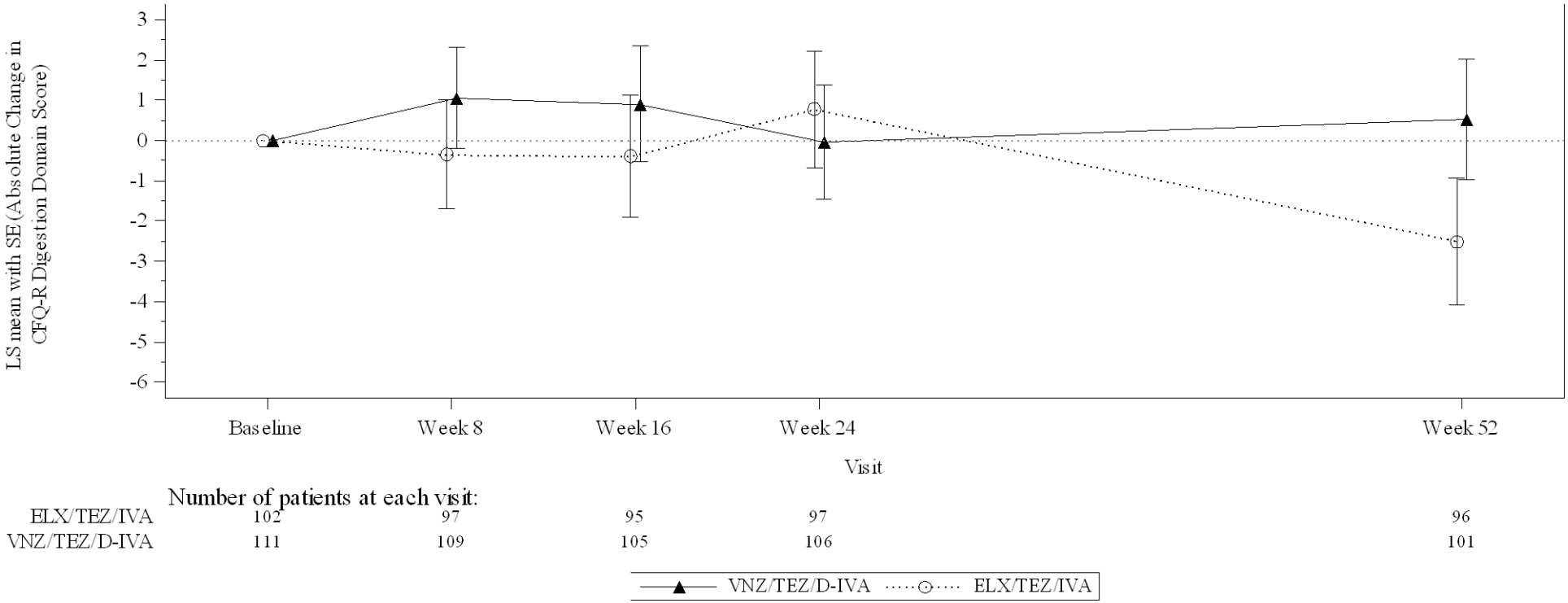
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America



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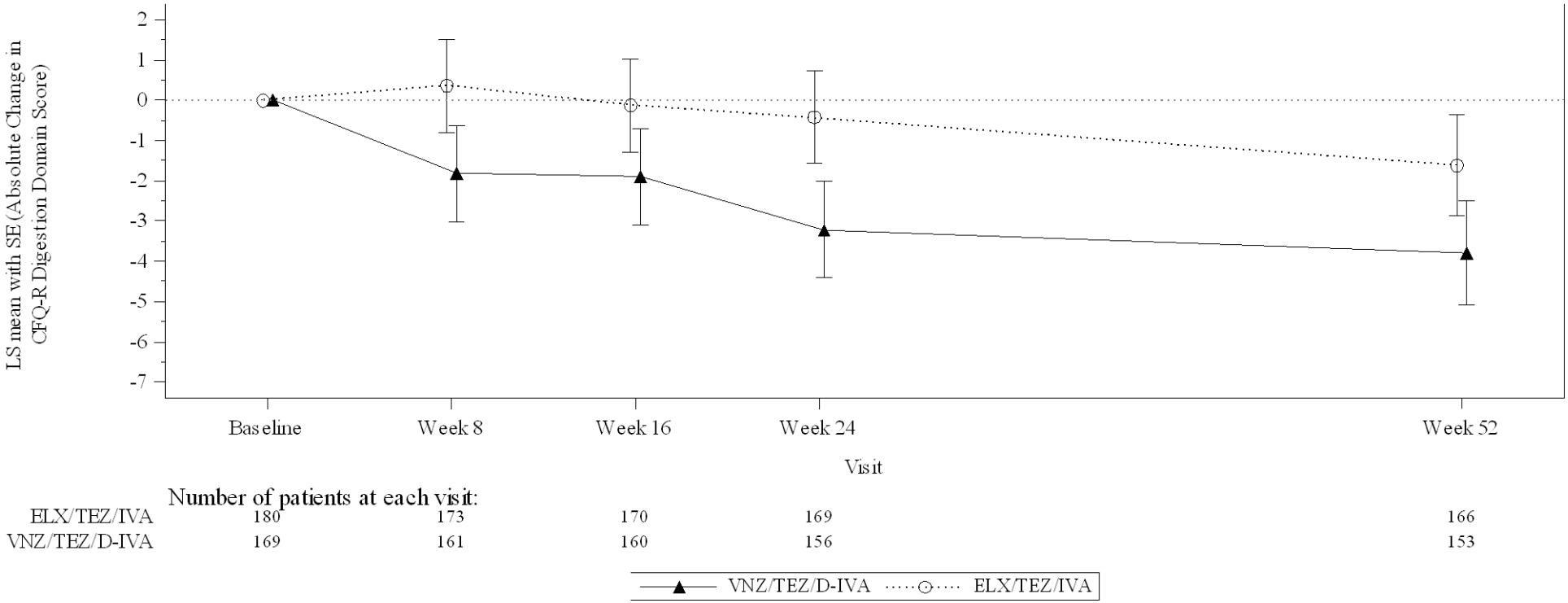
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World



Number of patients at each visit:

ELX/TEZ/IVA	180	173	170	169	166
VNZ/TEZ/D-IVA	169	161	160	156	153

VNZ/TEZ/D-IVA ELX/TEZ/IVA

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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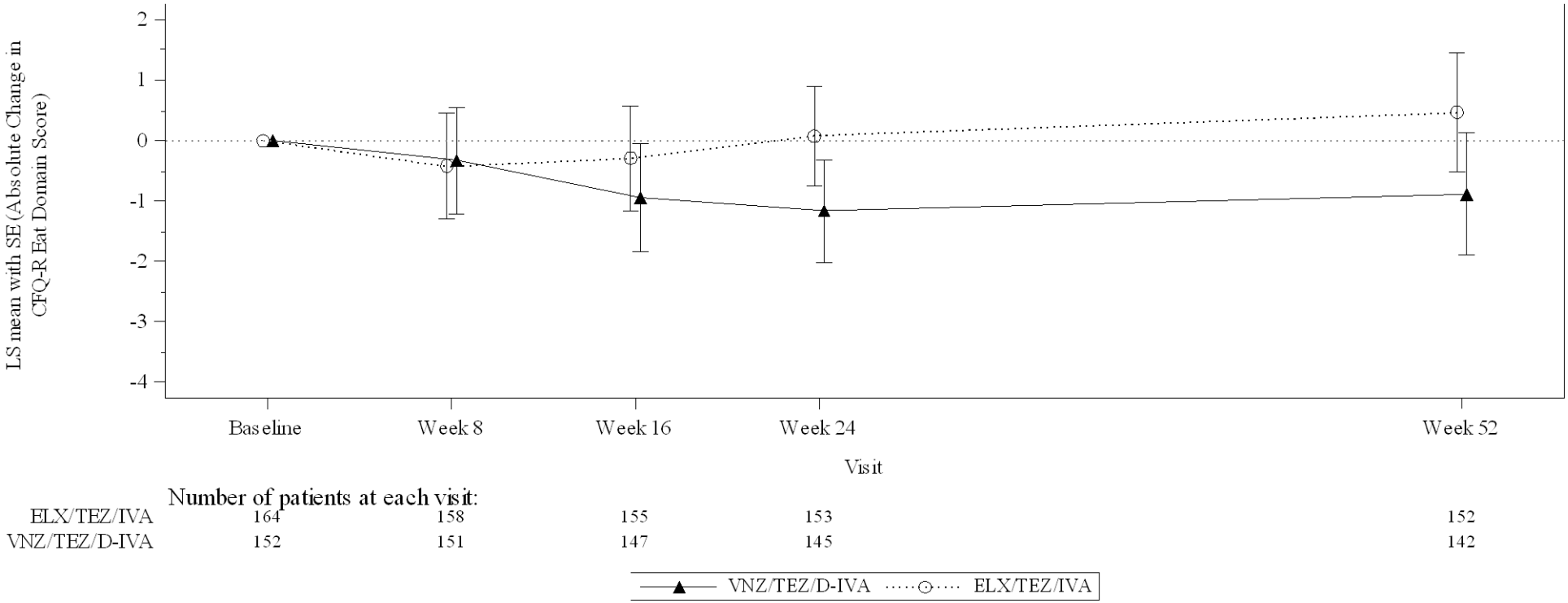
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
ppFEV$_1$ at baseline <70 %



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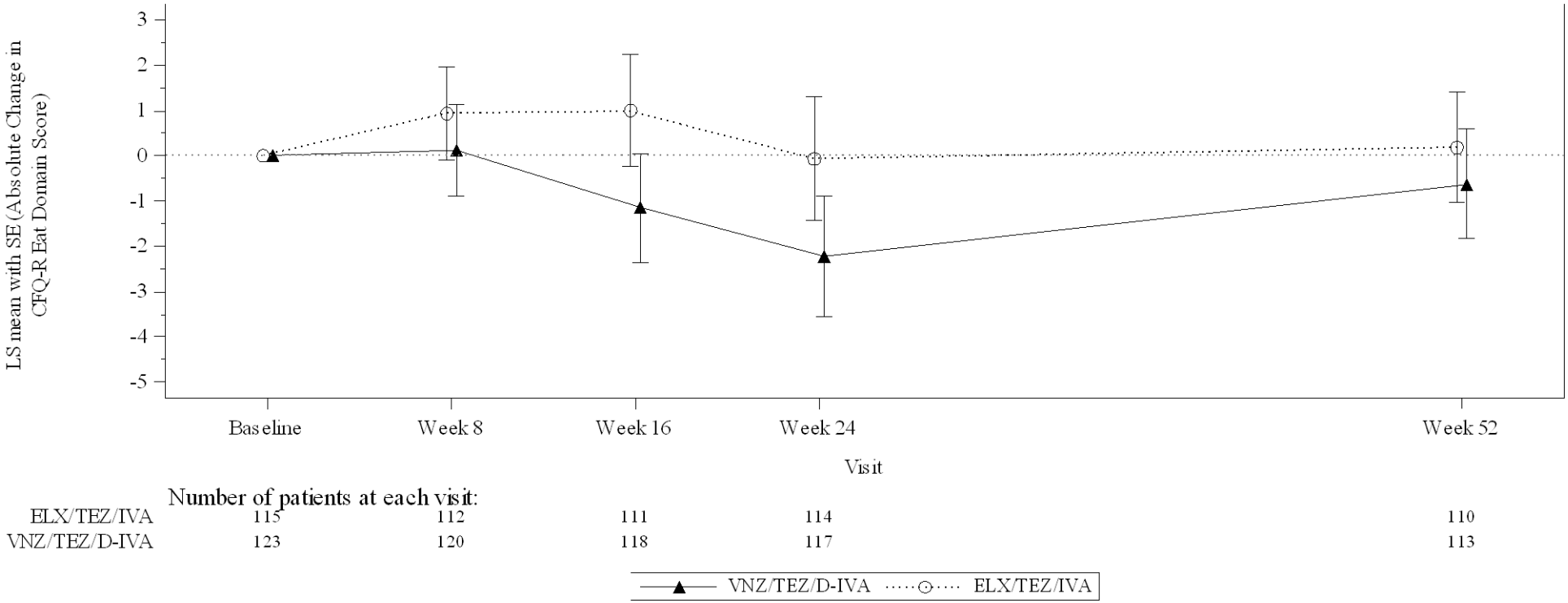
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
ppFEV$_1$ at baseline ≥70 %



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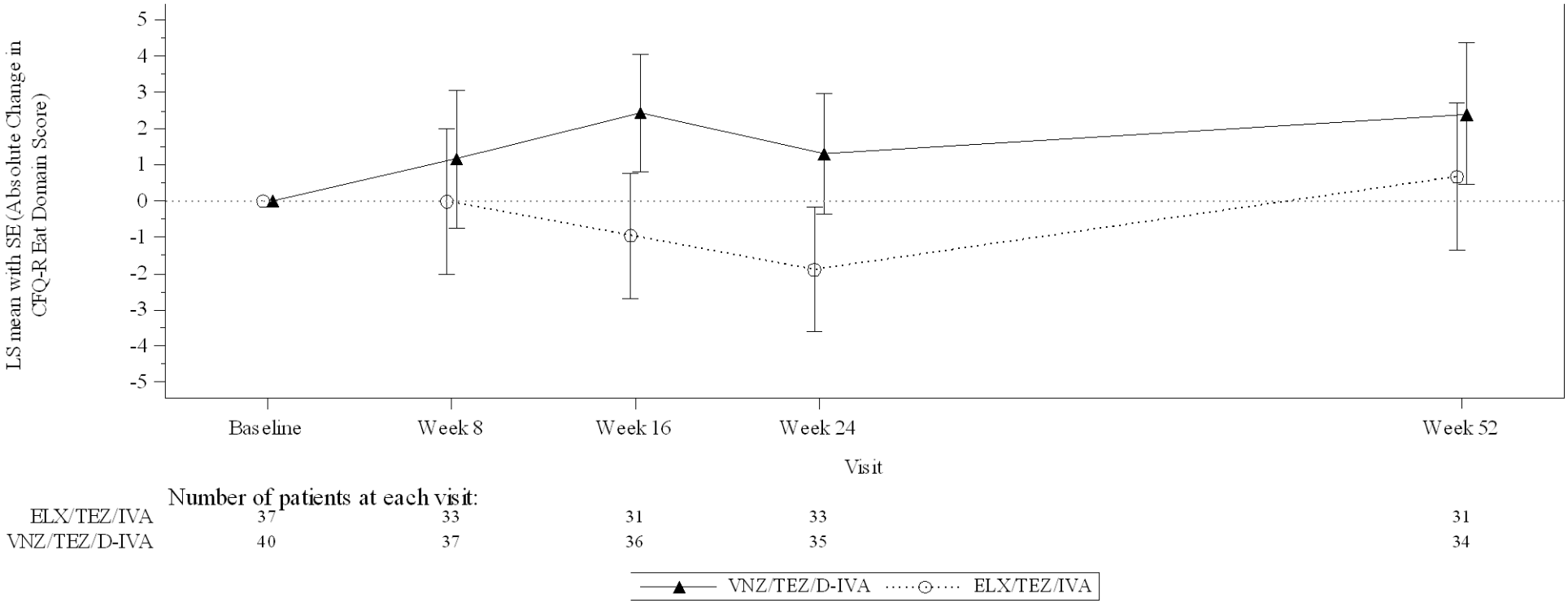
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years



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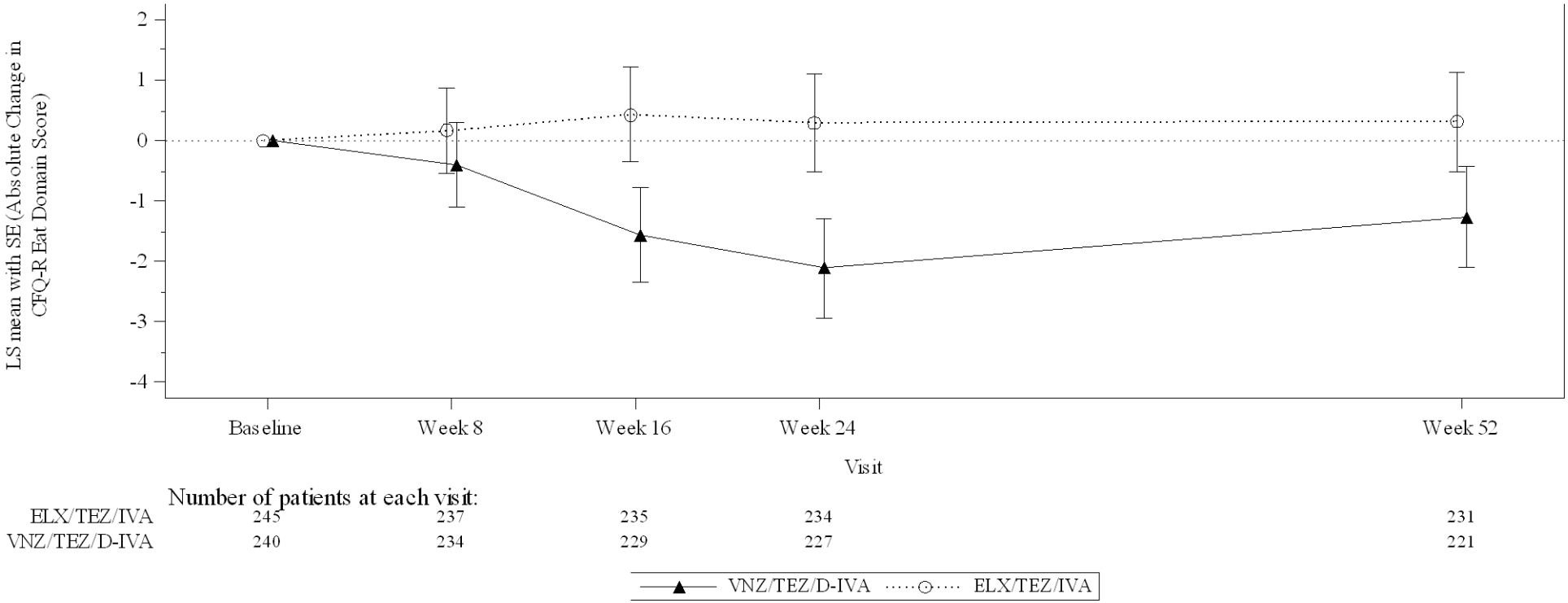
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years



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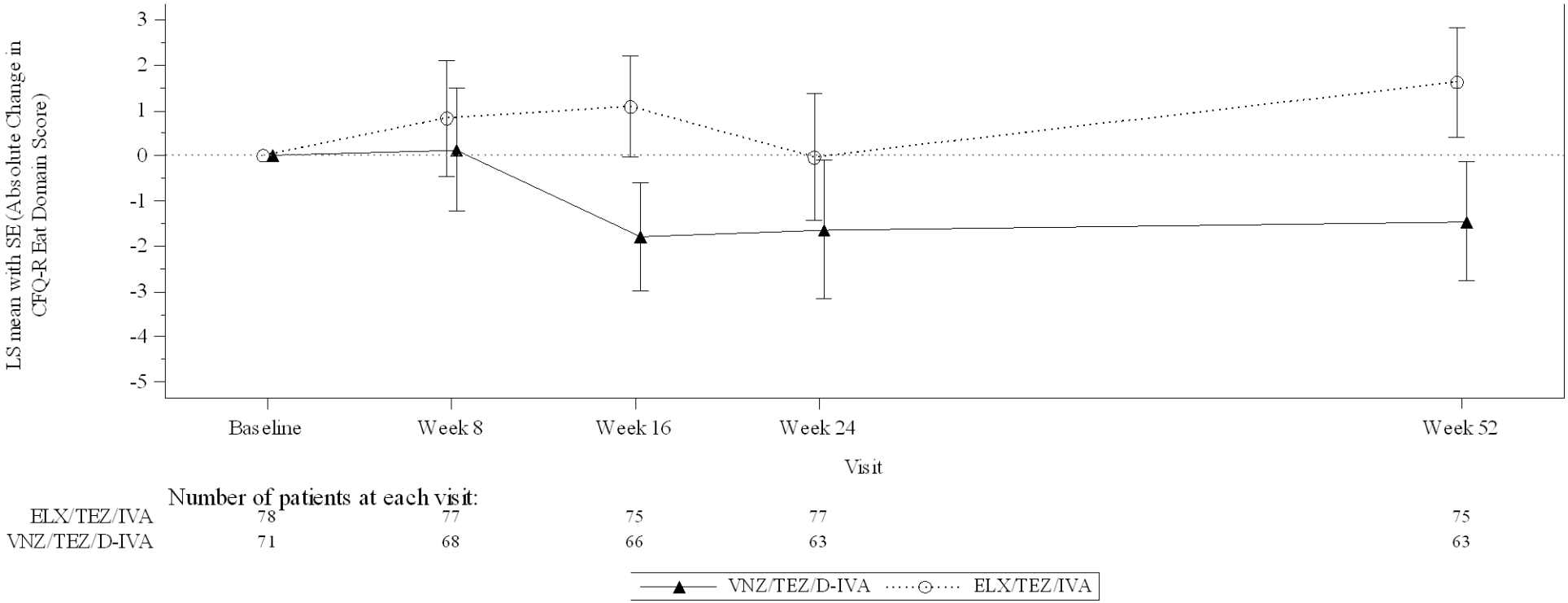
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L



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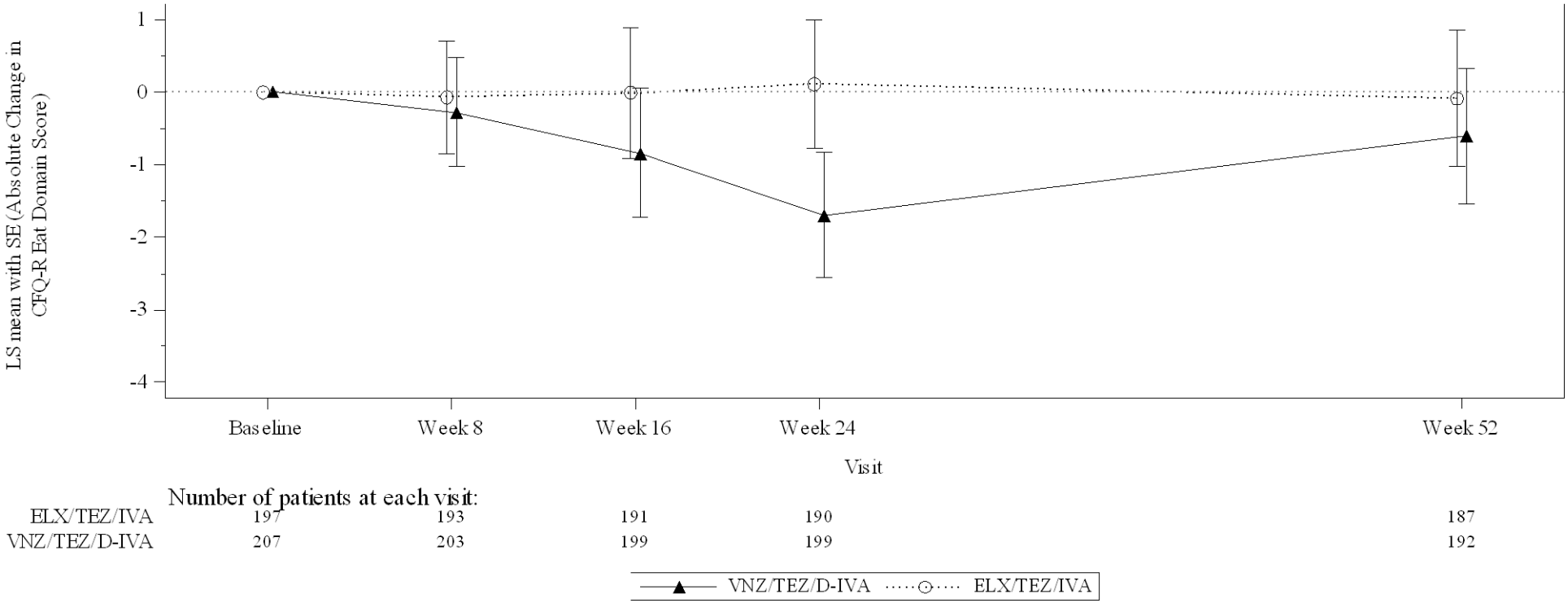
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L



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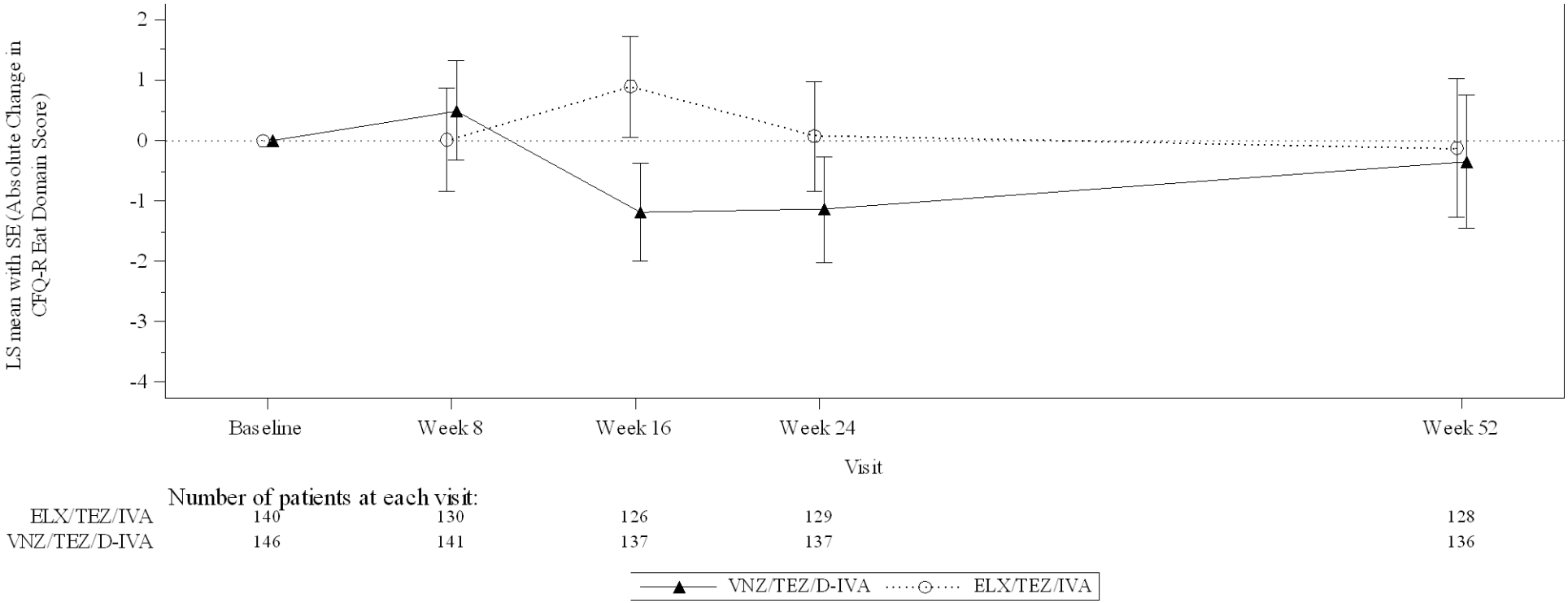
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male



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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

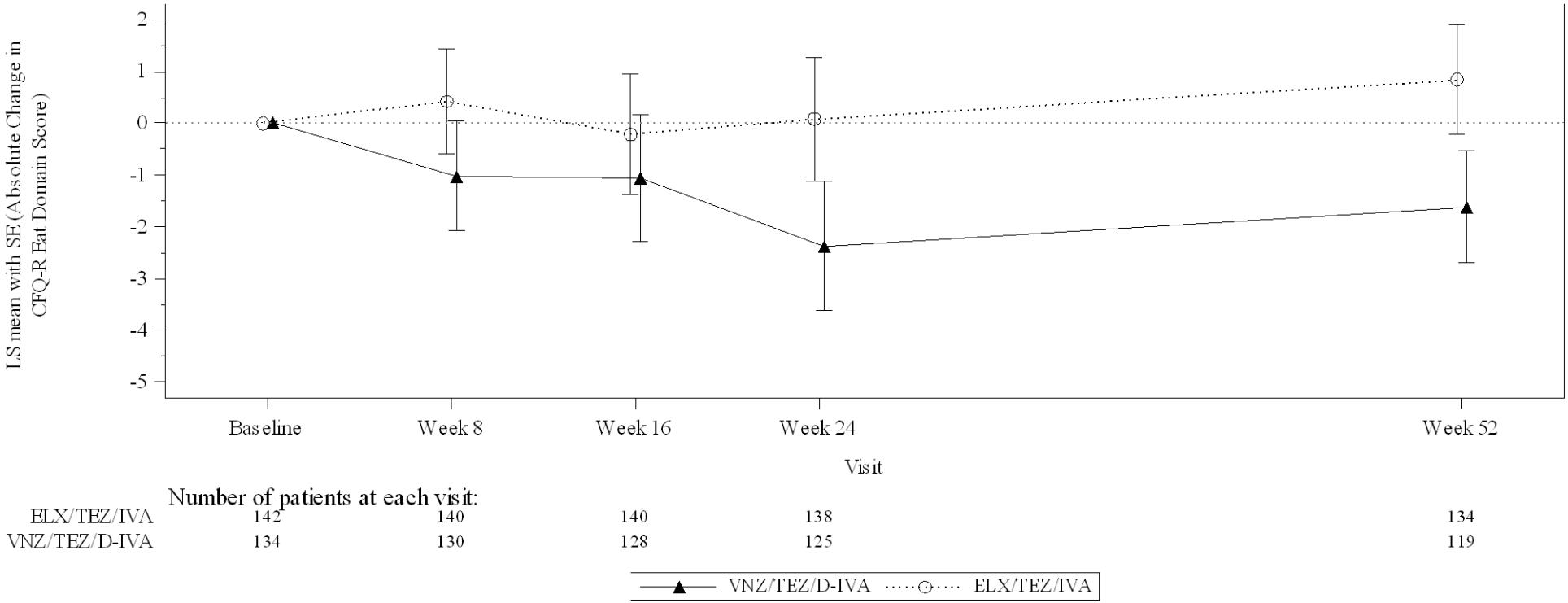

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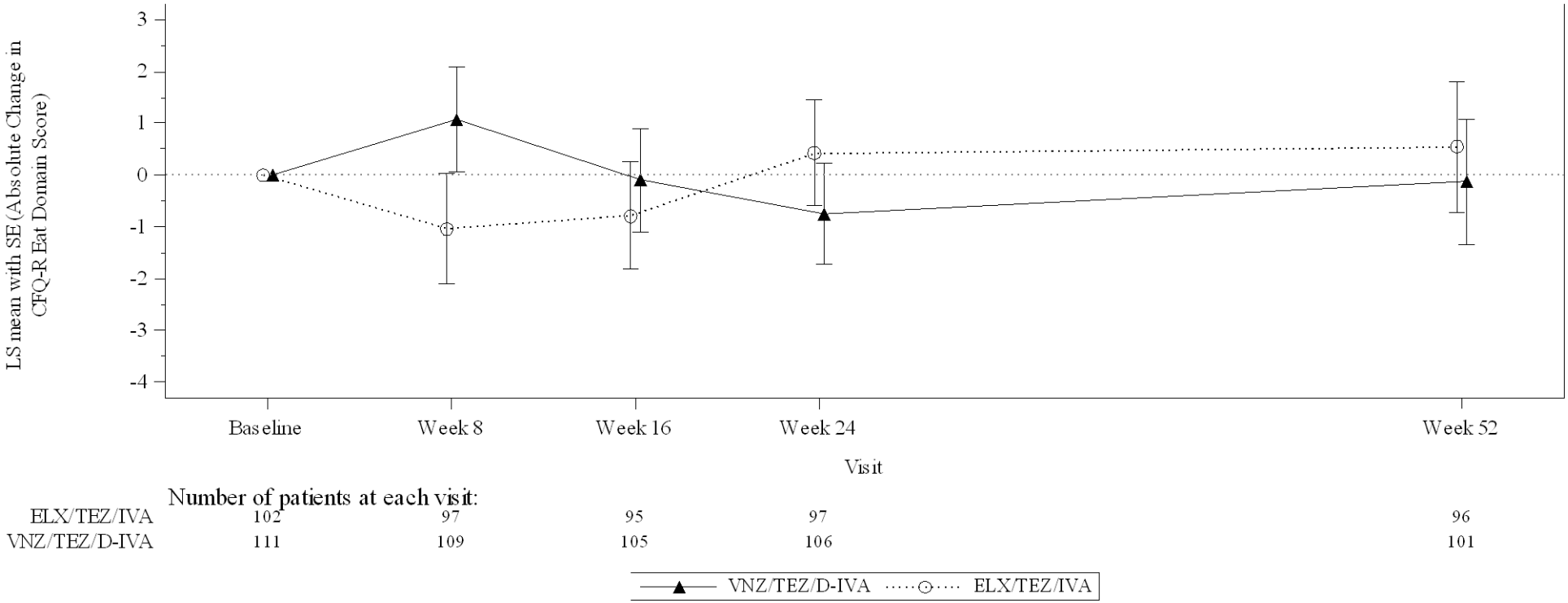
Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America



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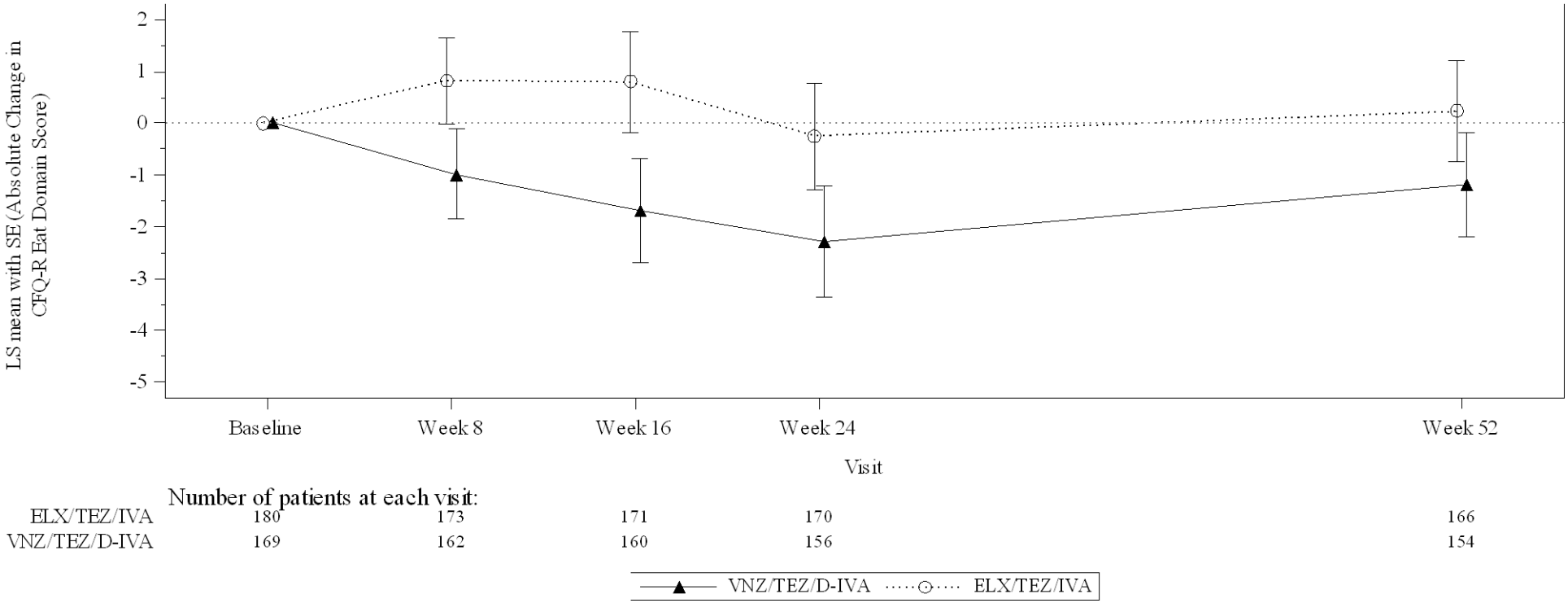
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World



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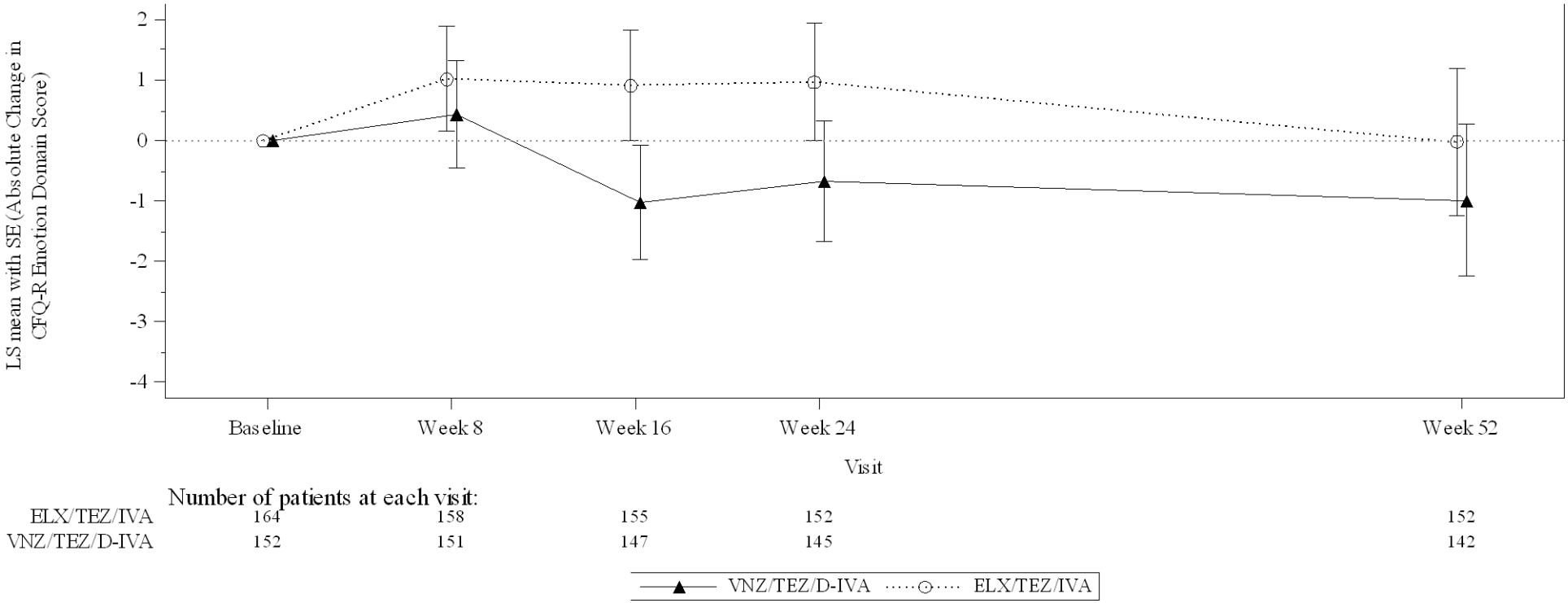
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
ppFEV$_1$ at baseline <70 %



Number of patients at each visit:

ELX/TEZ/IVA	164	158	155	152	152
VNZ/TEZ/D-IVA	152	151	147	145	142

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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
ppFEV$_1$ at baseline ≥70 %

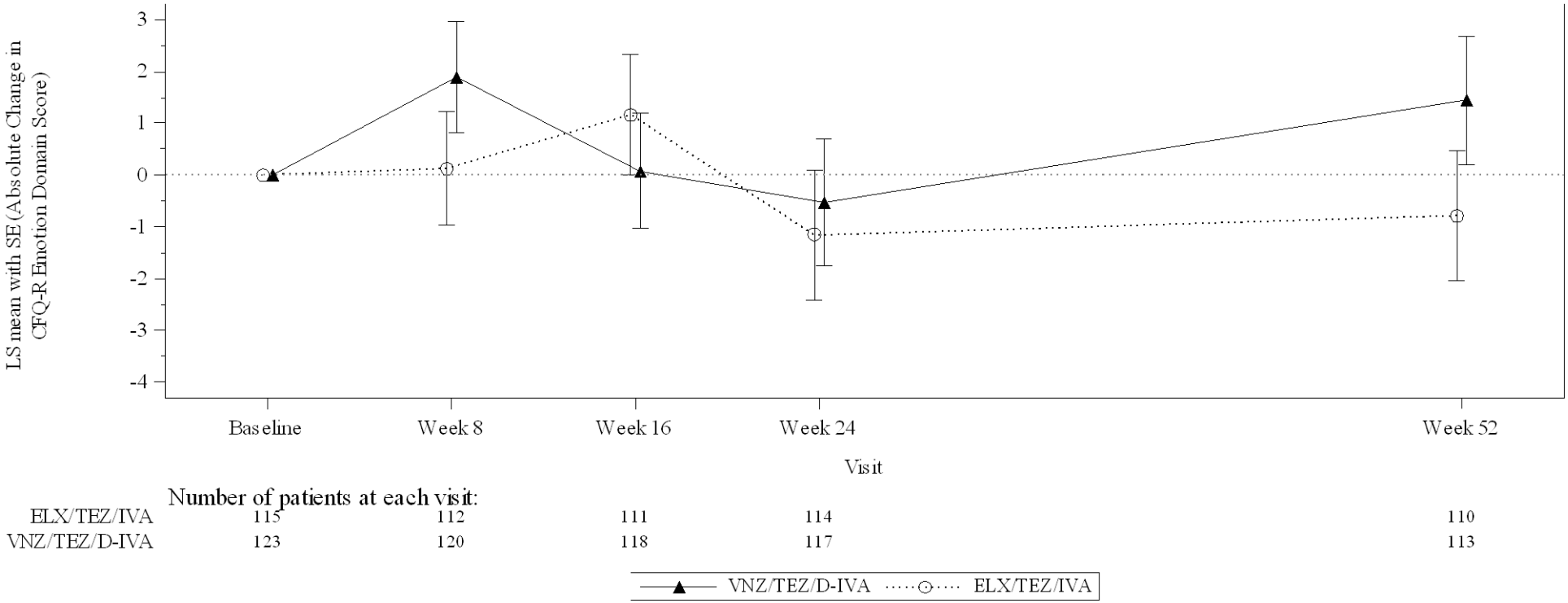

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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

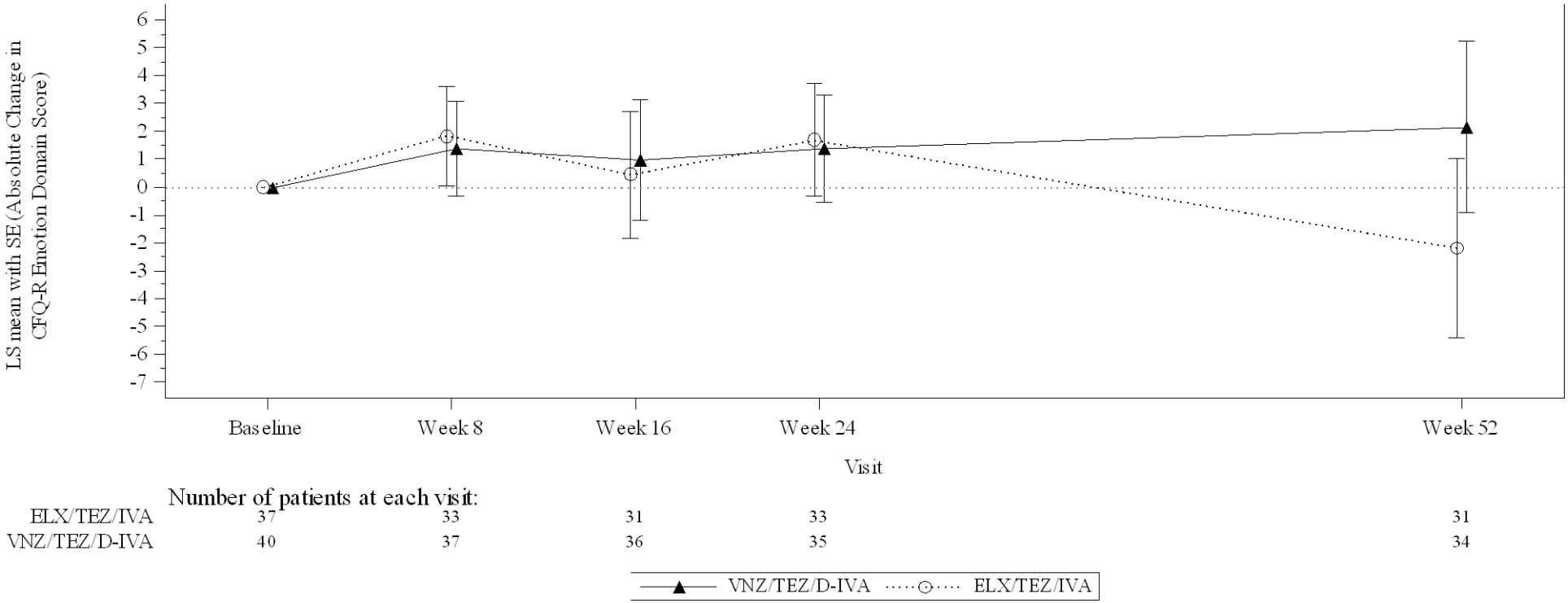

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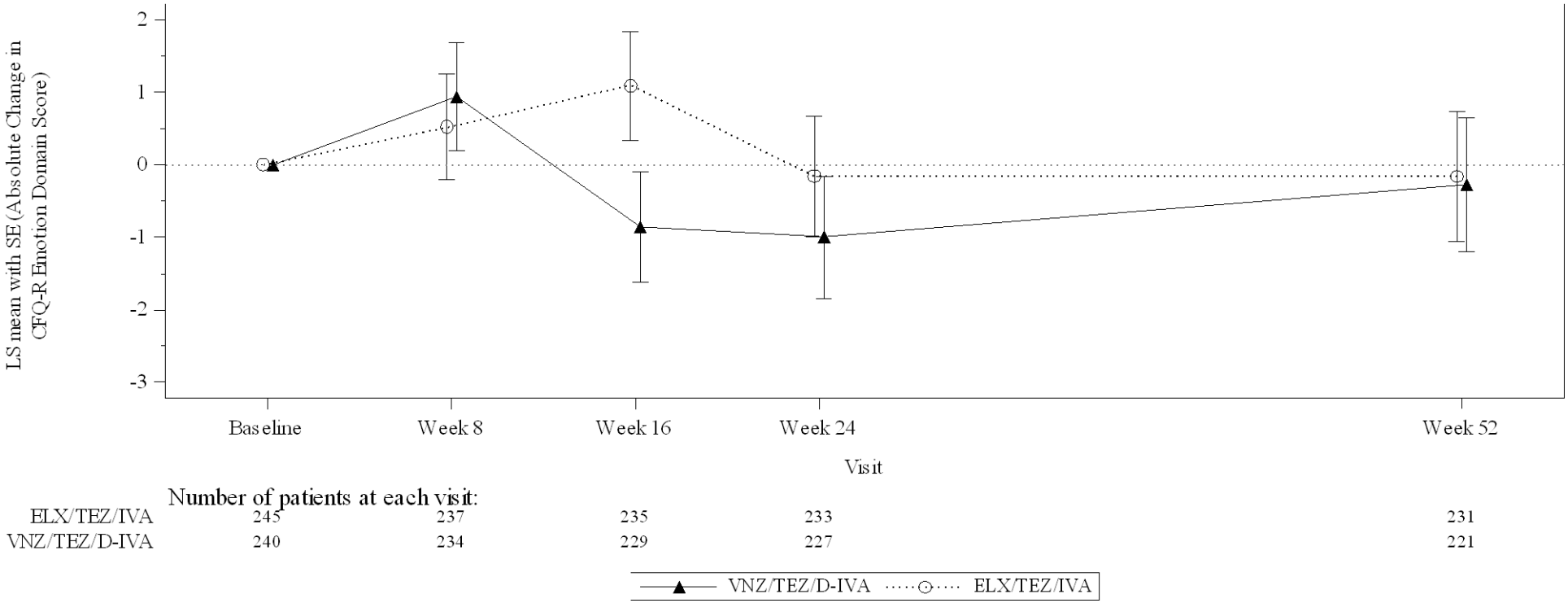
Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years



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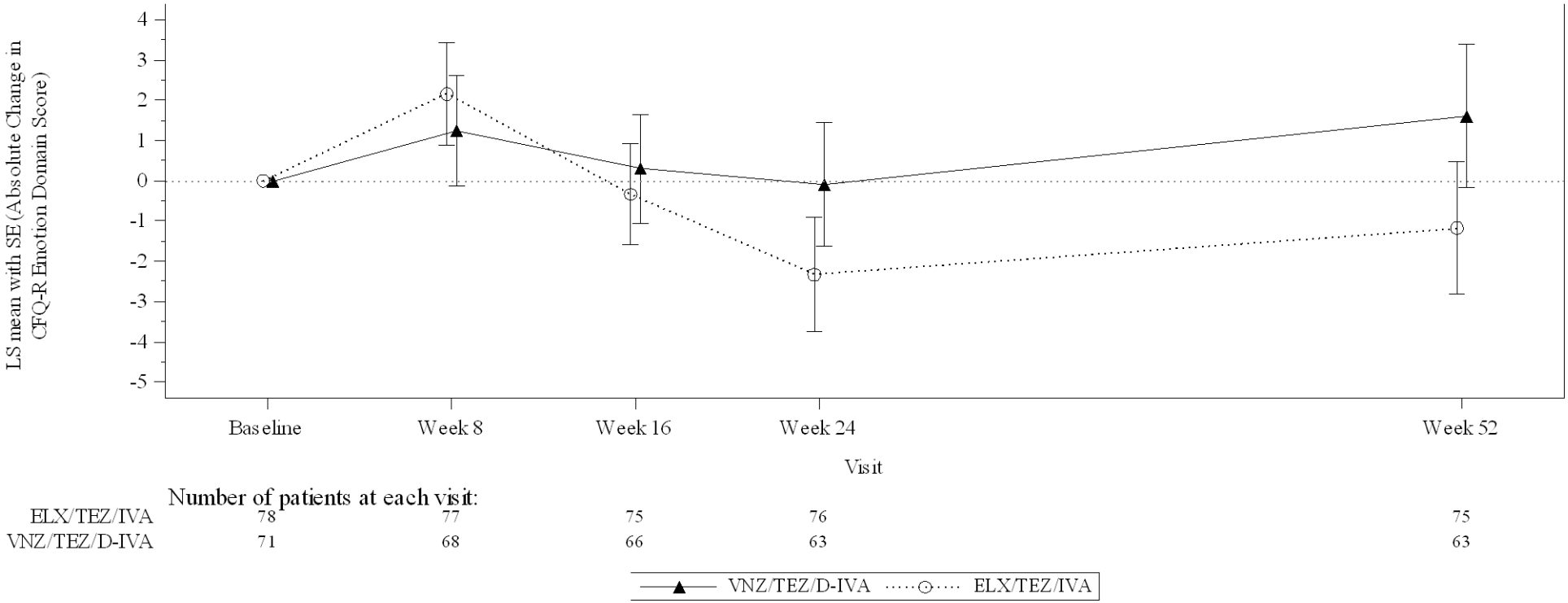
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L



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Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

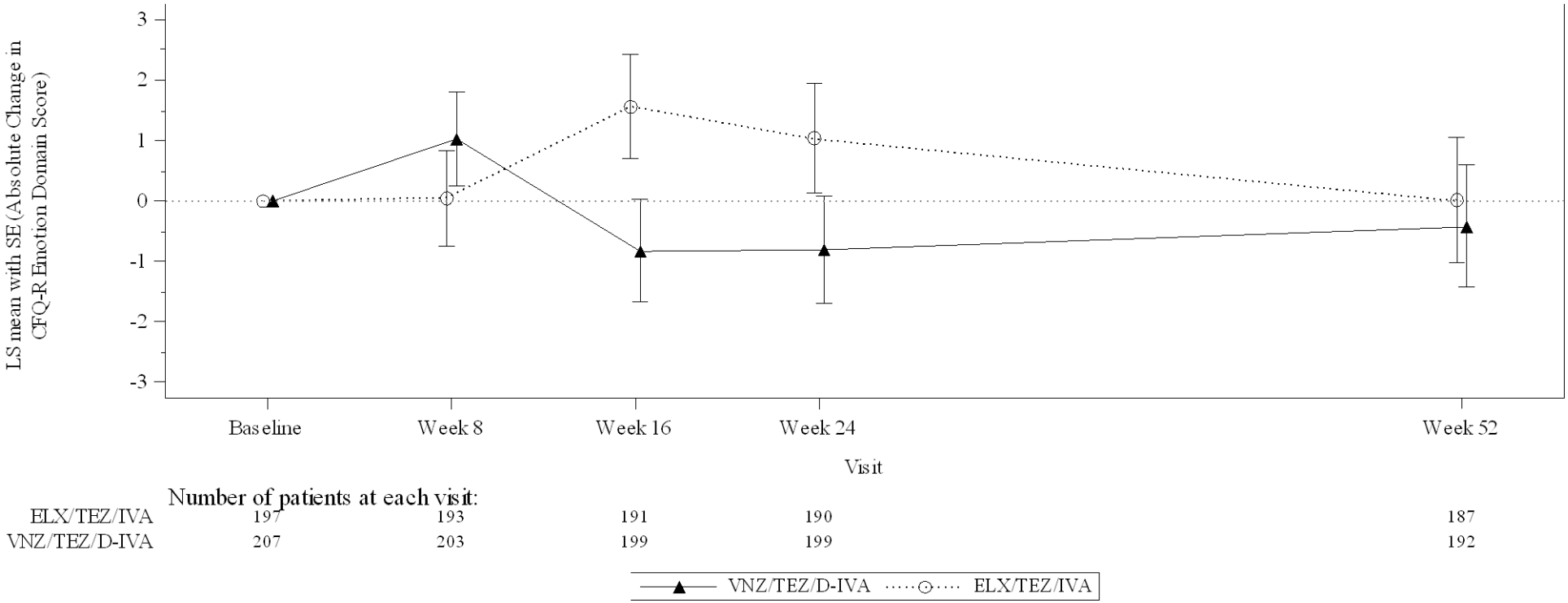

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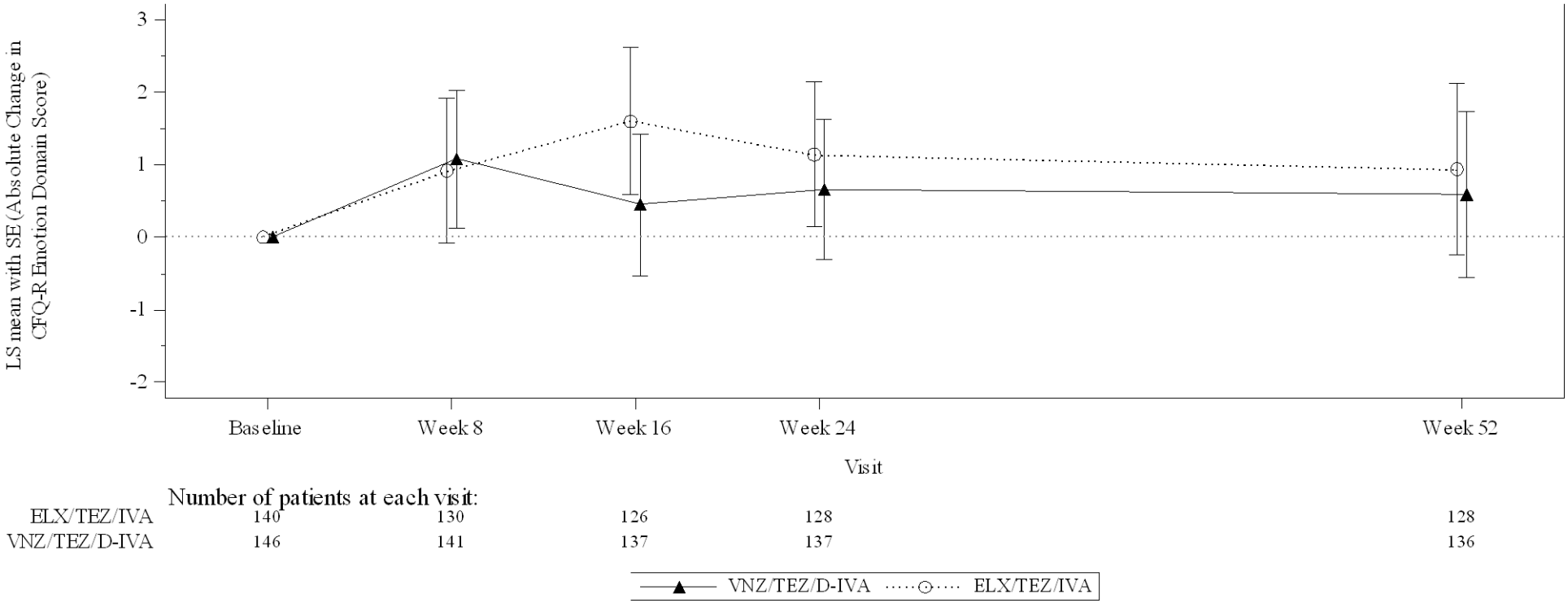
Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male



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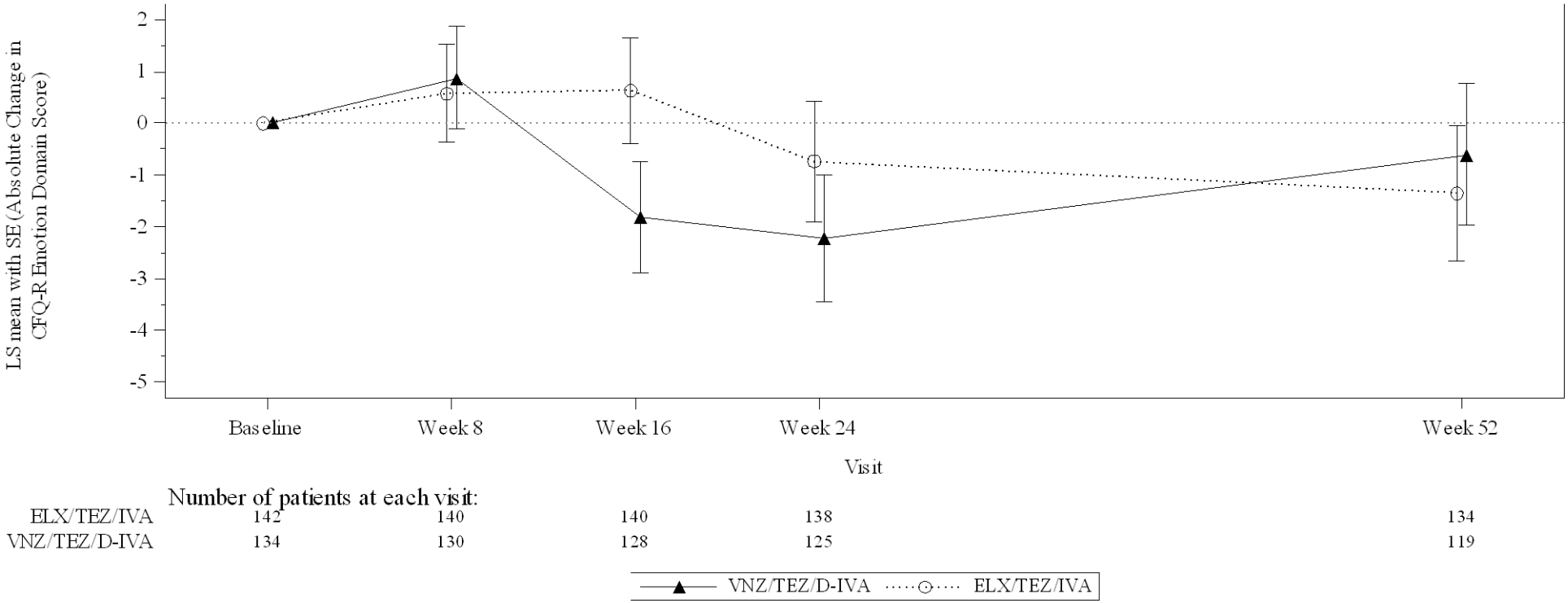
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female



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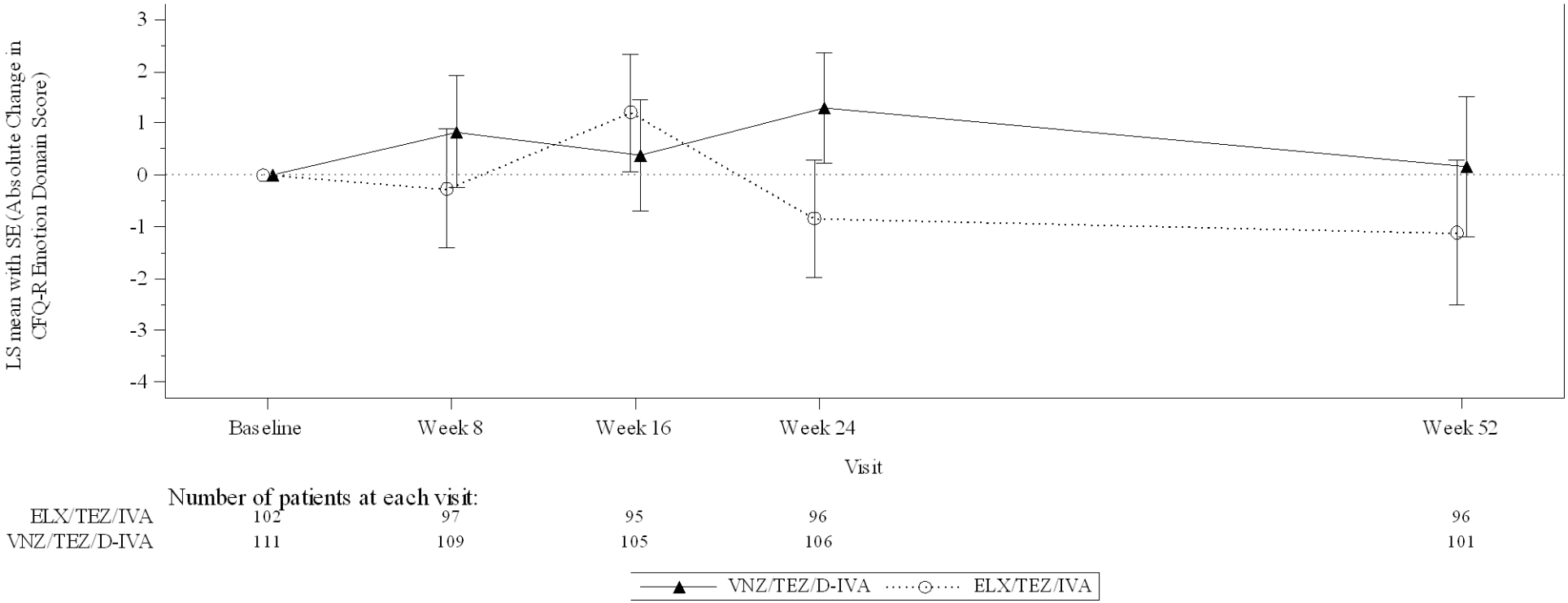
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America



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Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

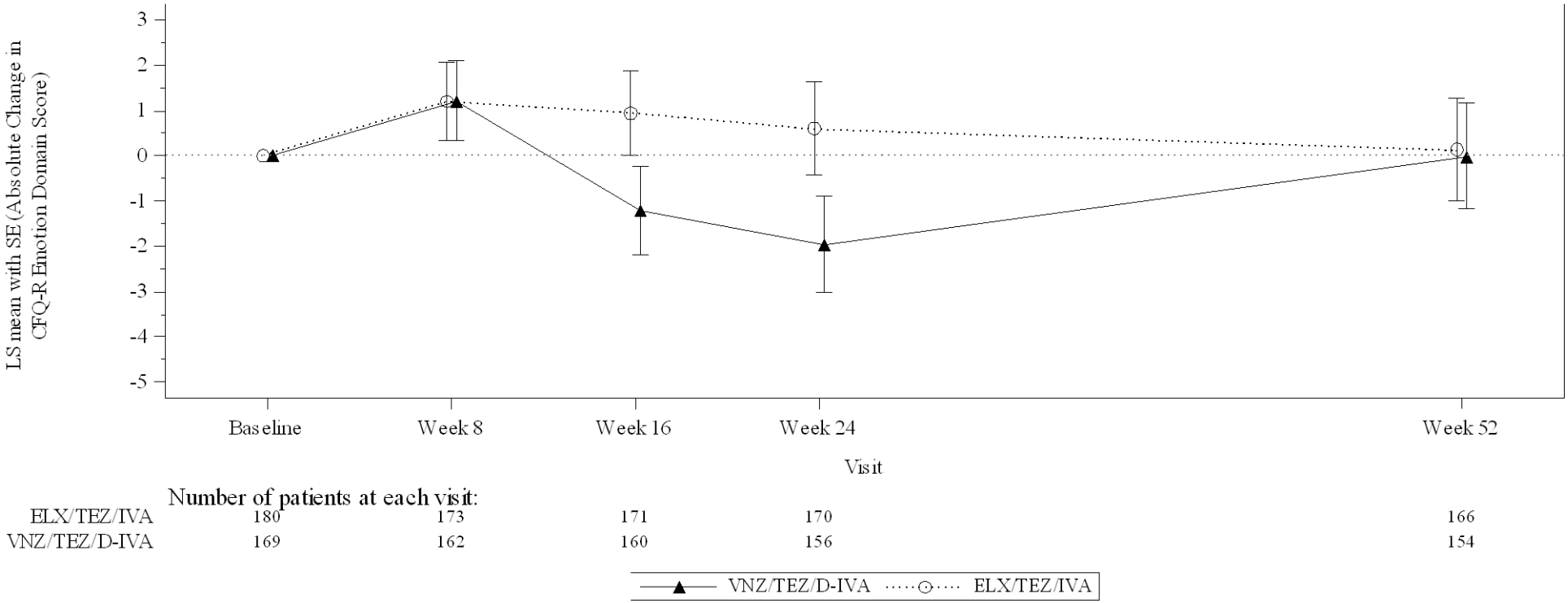

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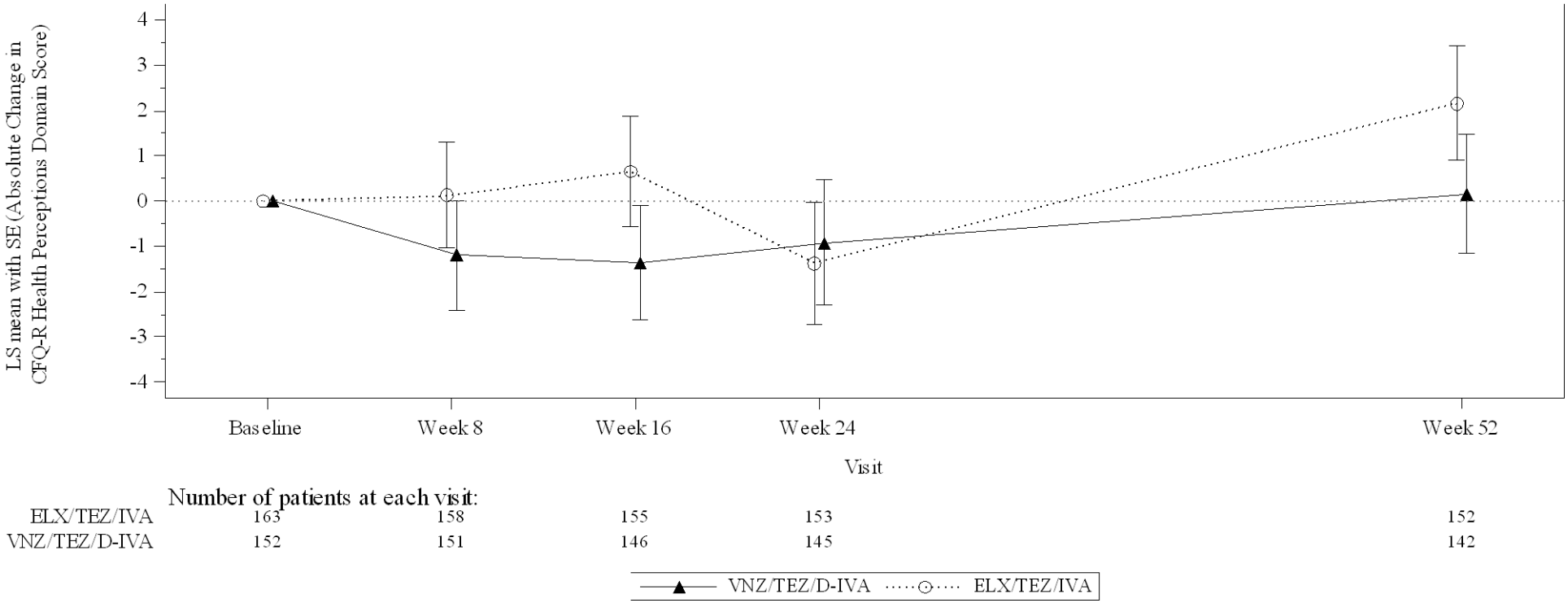
Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
ppFEV$_1$ at baseline <70 %



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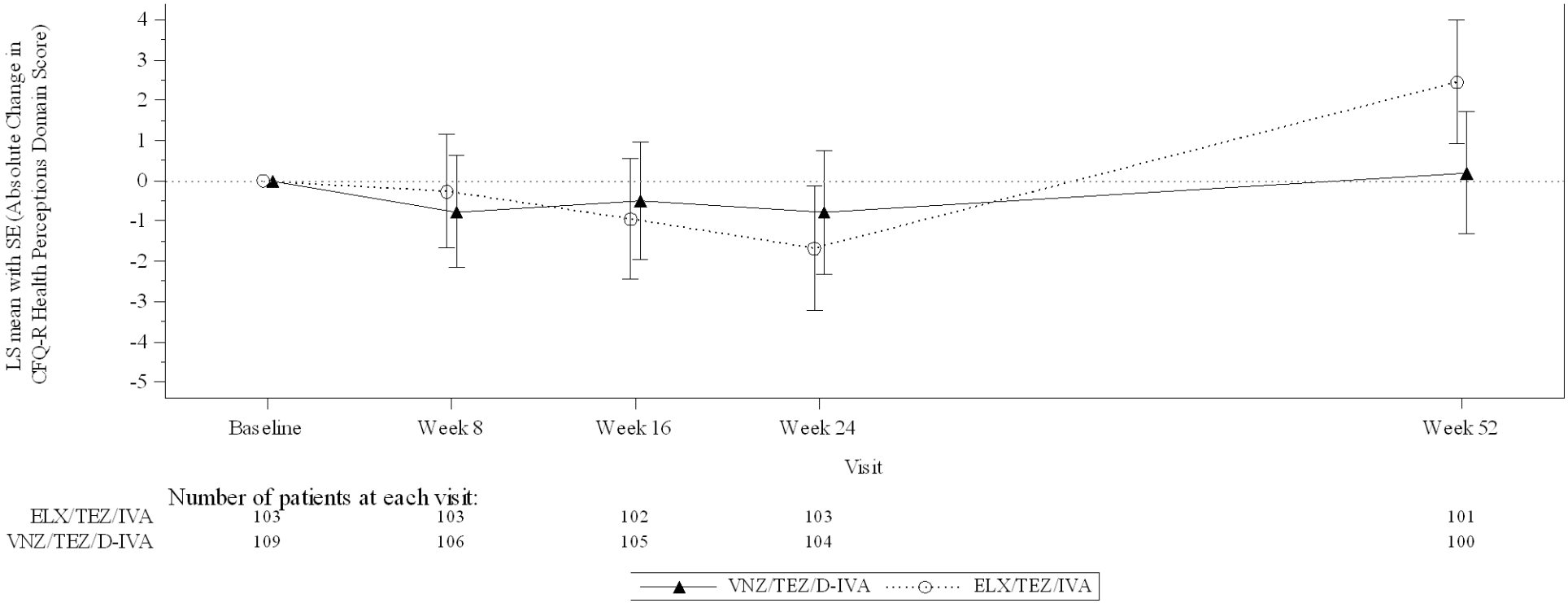
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
ppFEV$_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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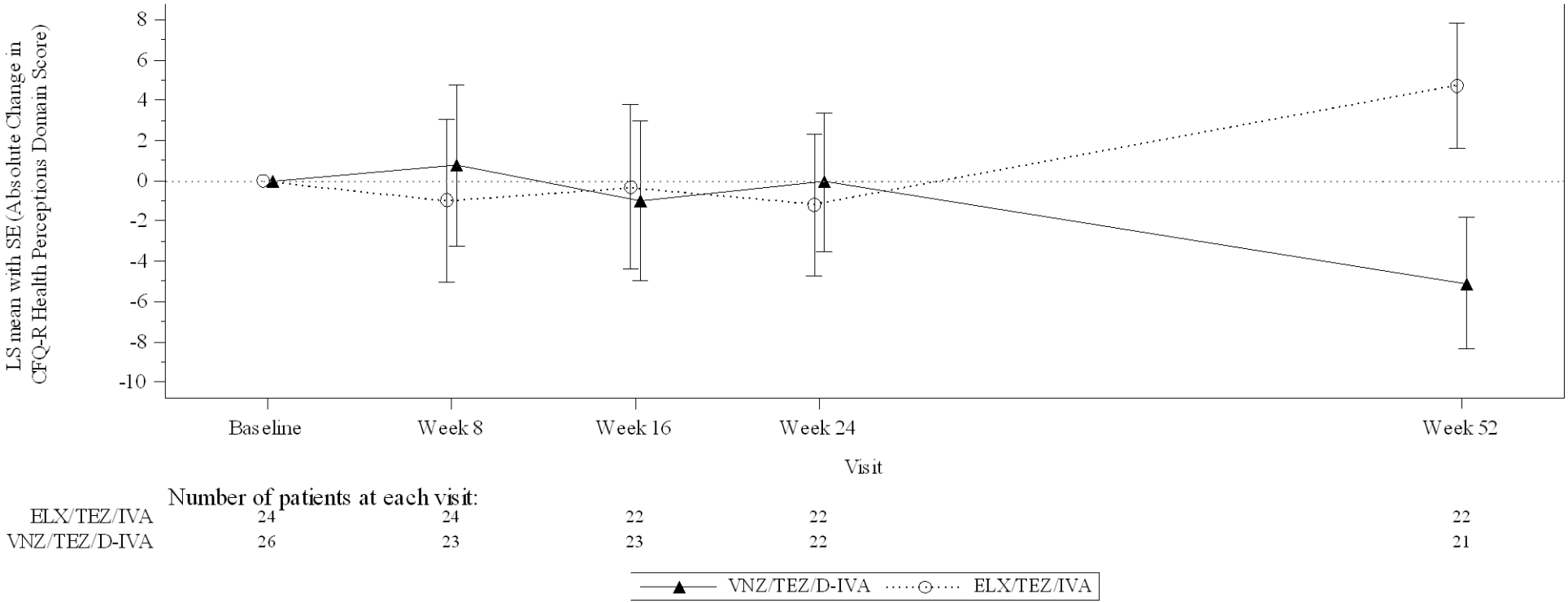
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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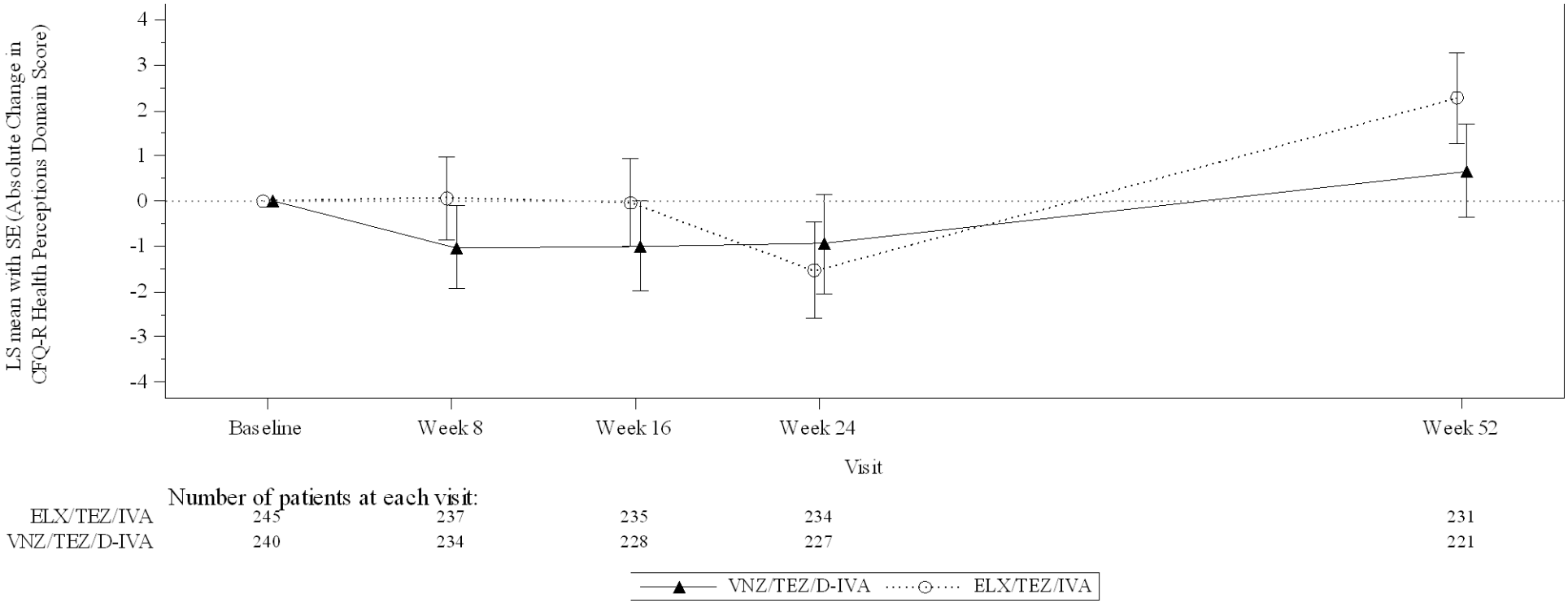
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years



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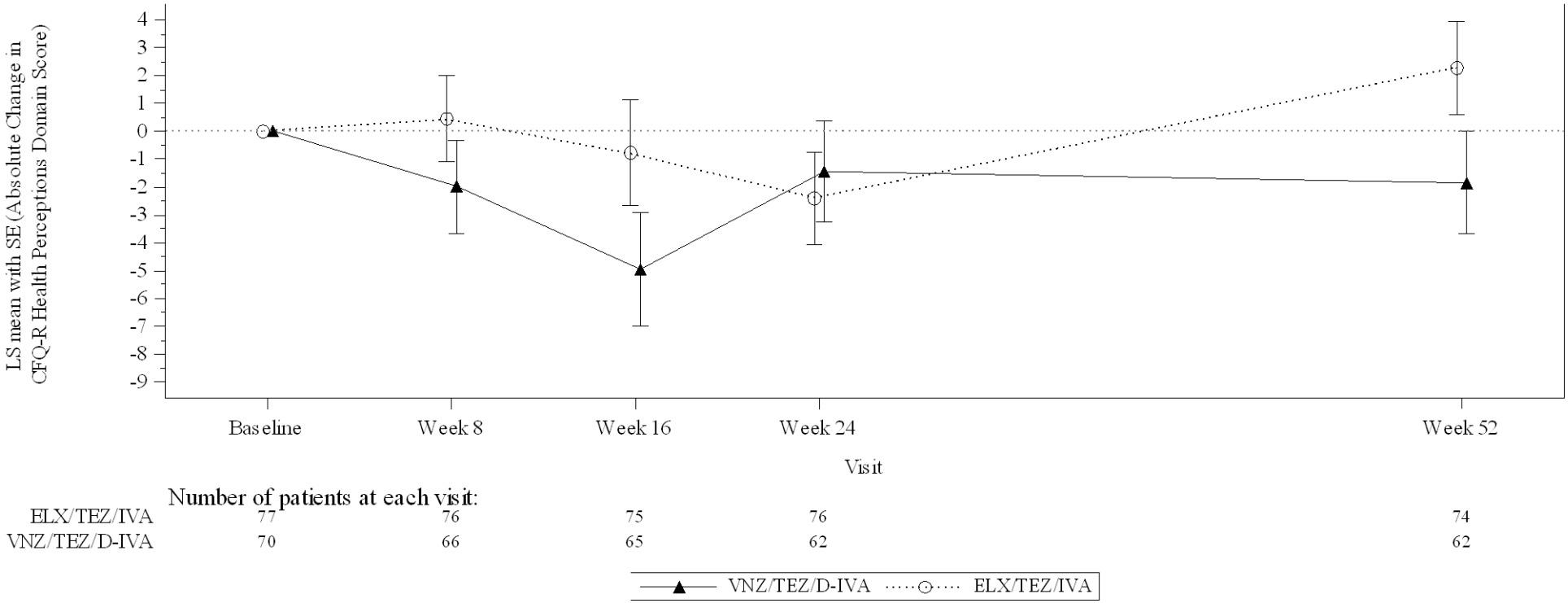
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L



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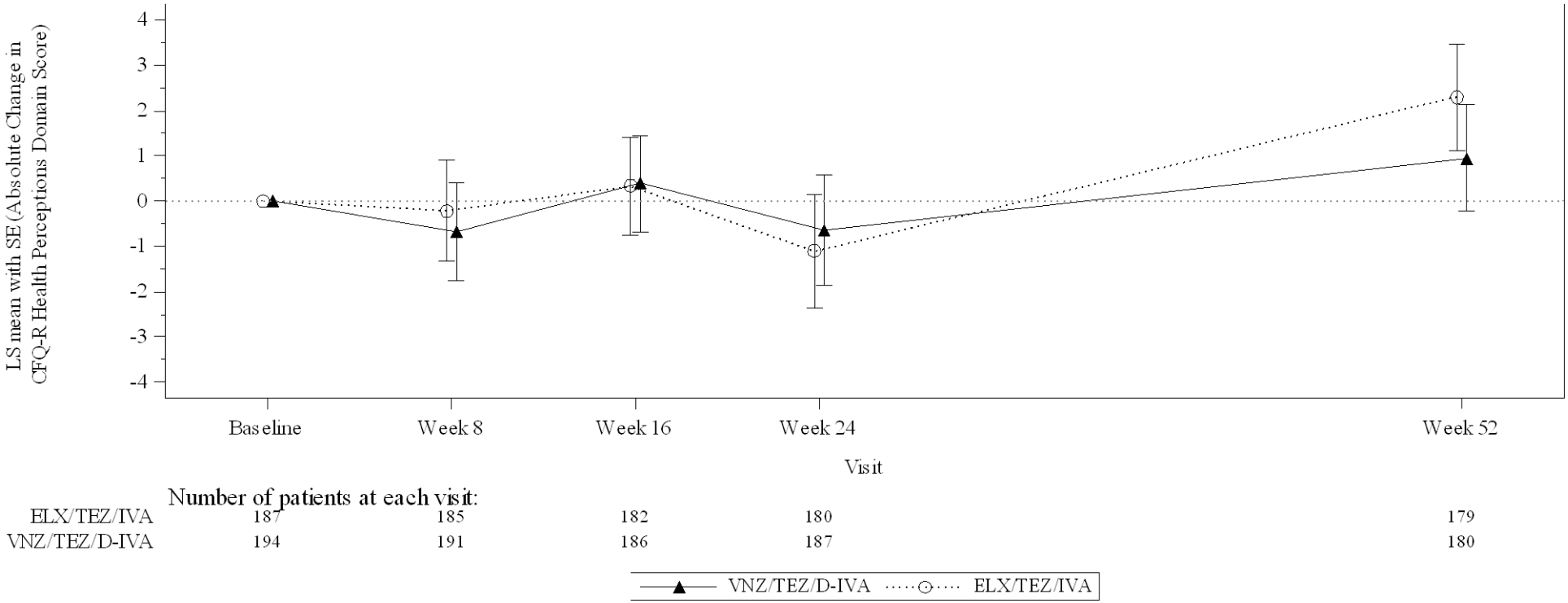
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

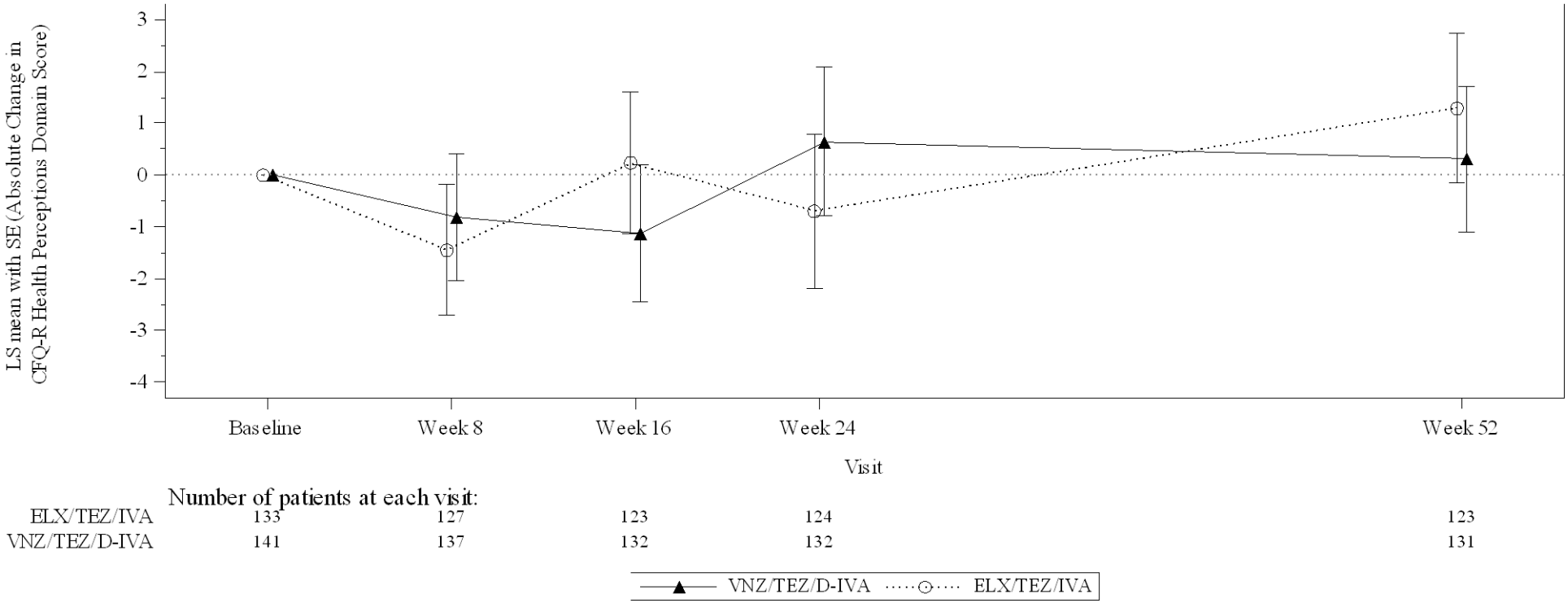


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male



Number of patients at each visit:

ELX/TEZ/IVA	133	127	123	124	123
VNZ/TEZ/D-IVA	141	137	132	132	131

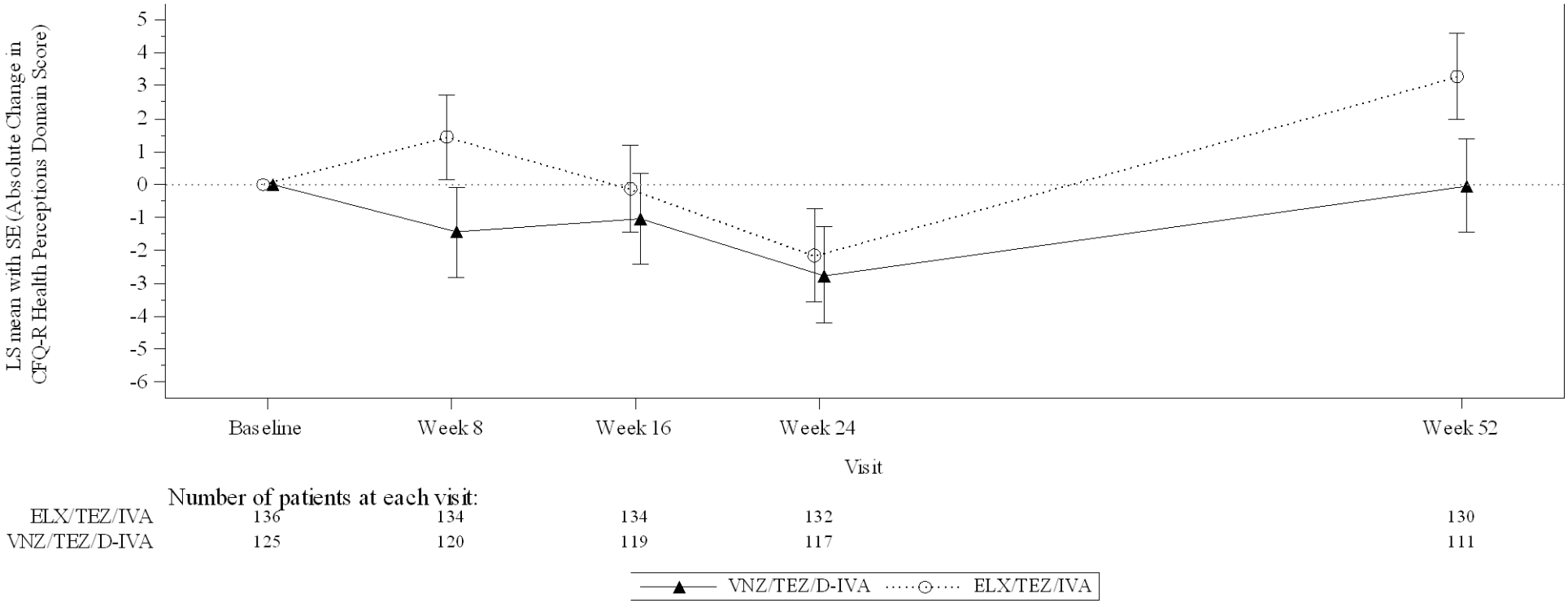
VNZ/TEZ/D-IVA ELX/TEZ/IVA

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female



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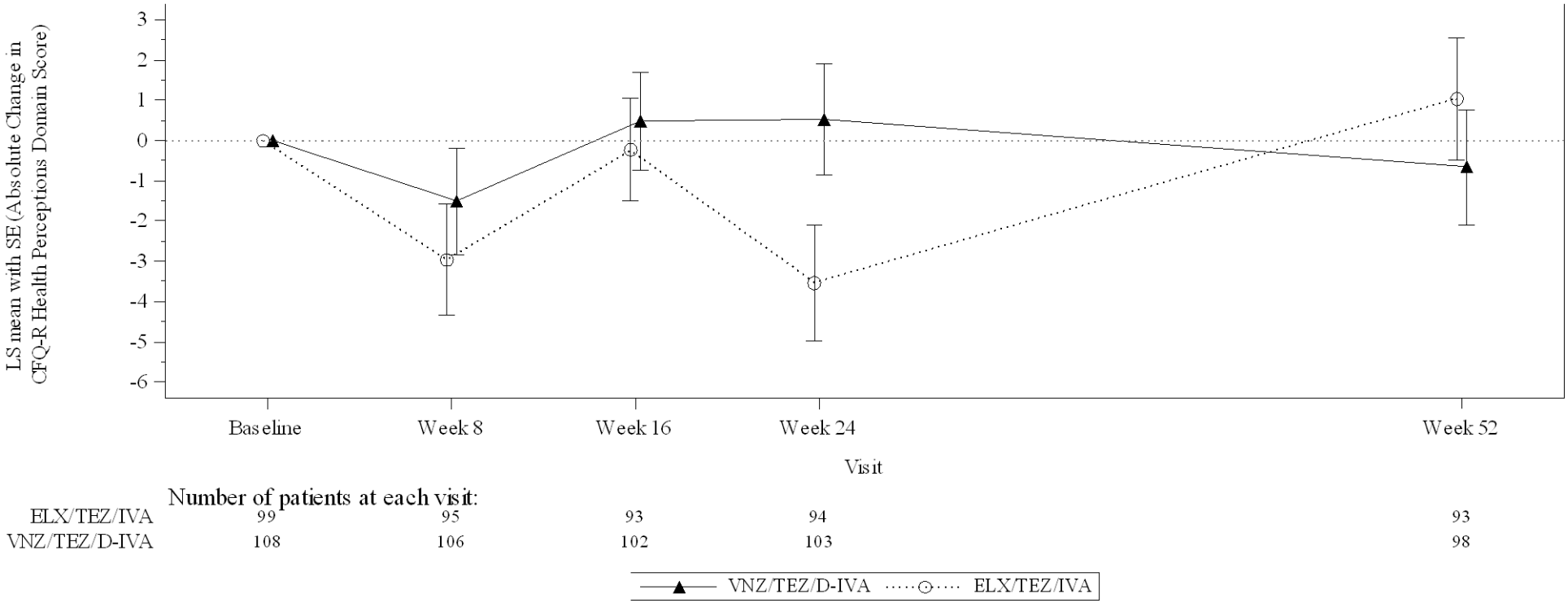
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America



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- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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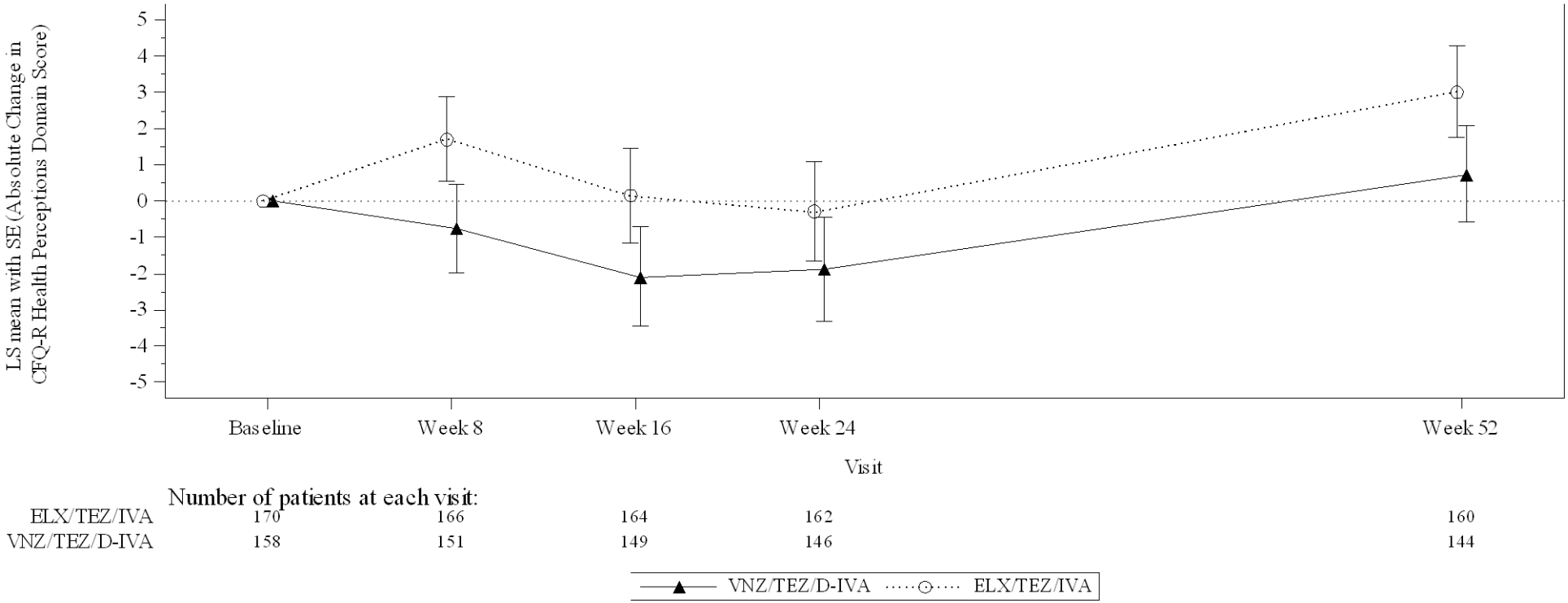
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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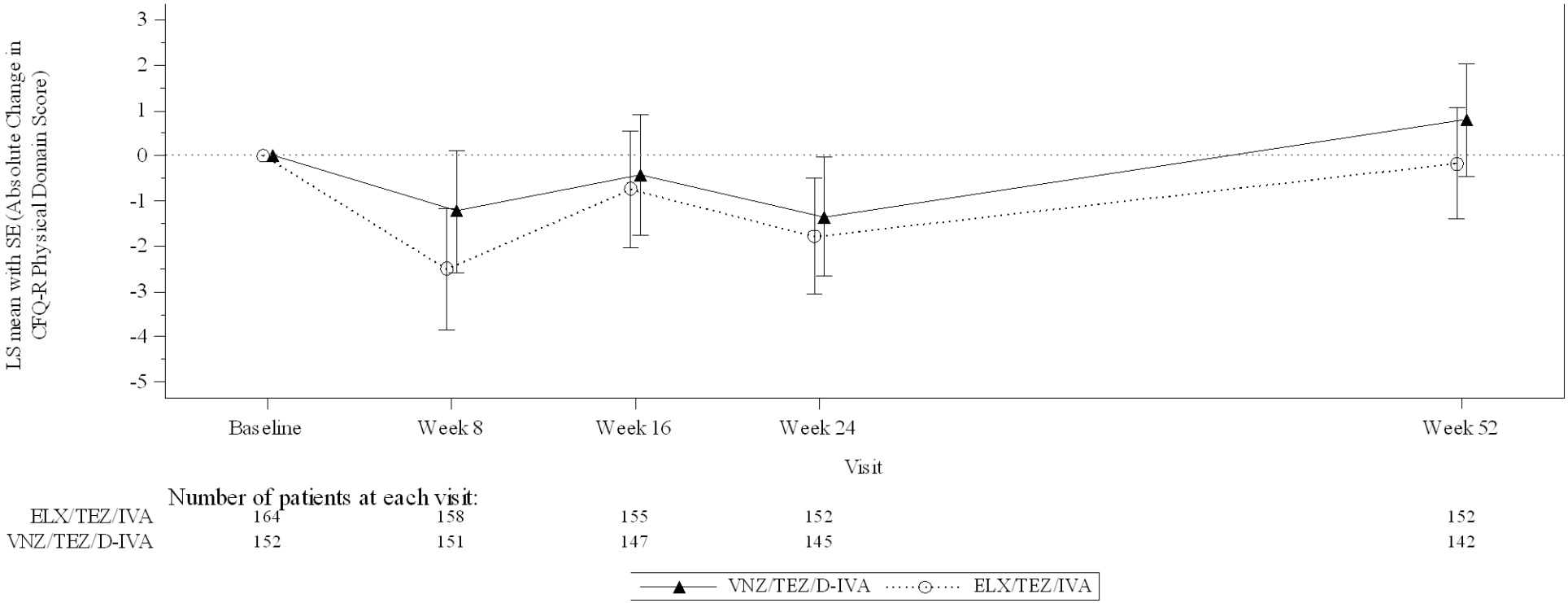
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
ppFEV$_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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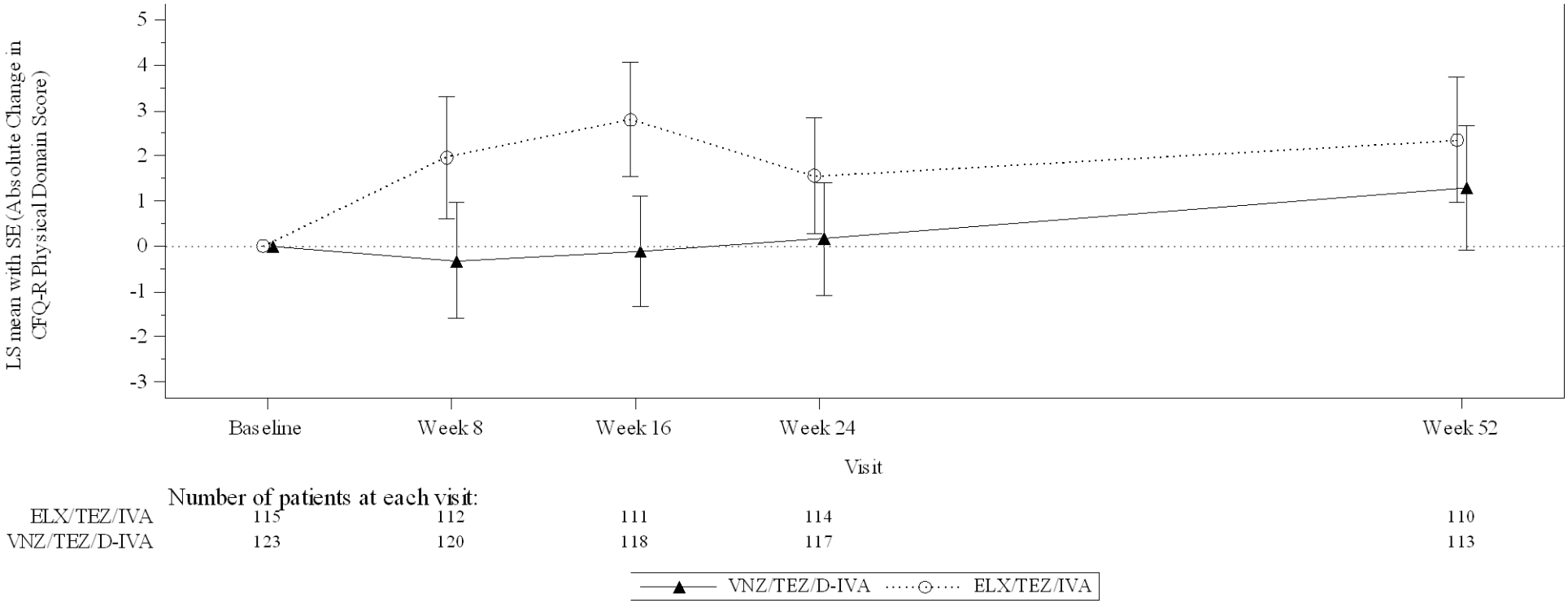
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
ppFEV$_1$ at baseline ≥70 %



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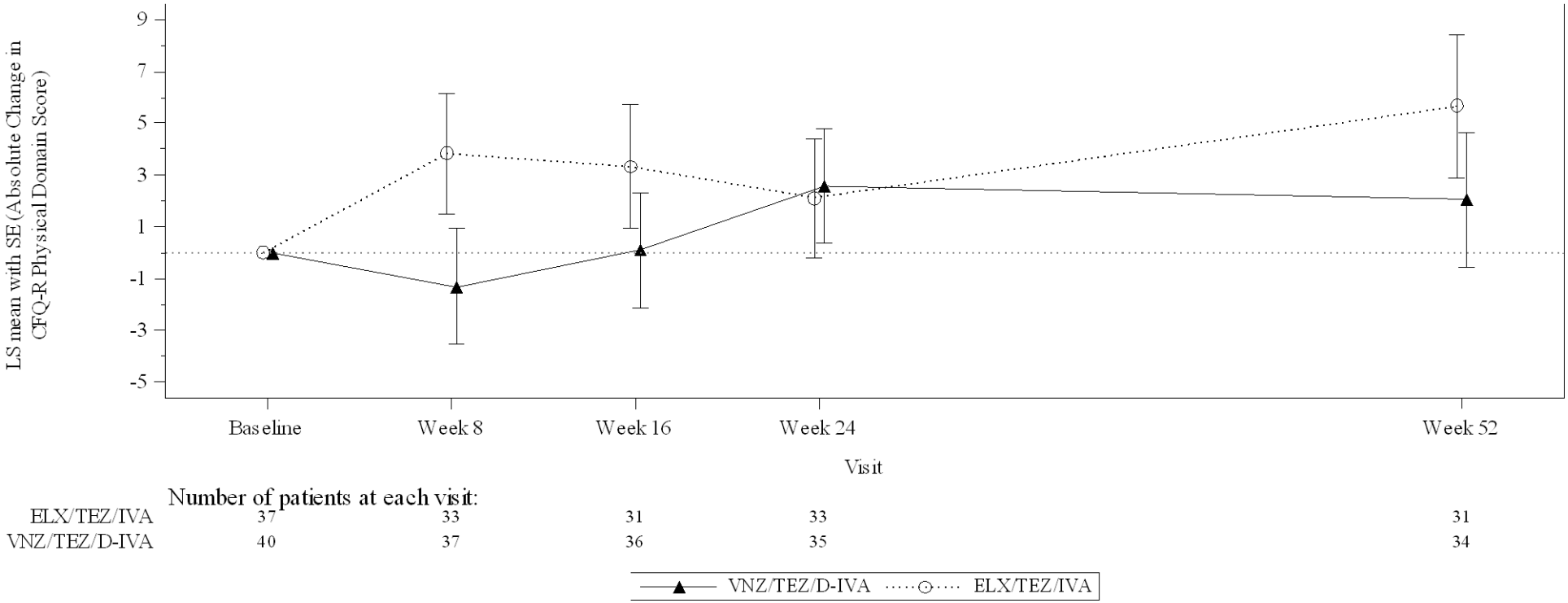
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years



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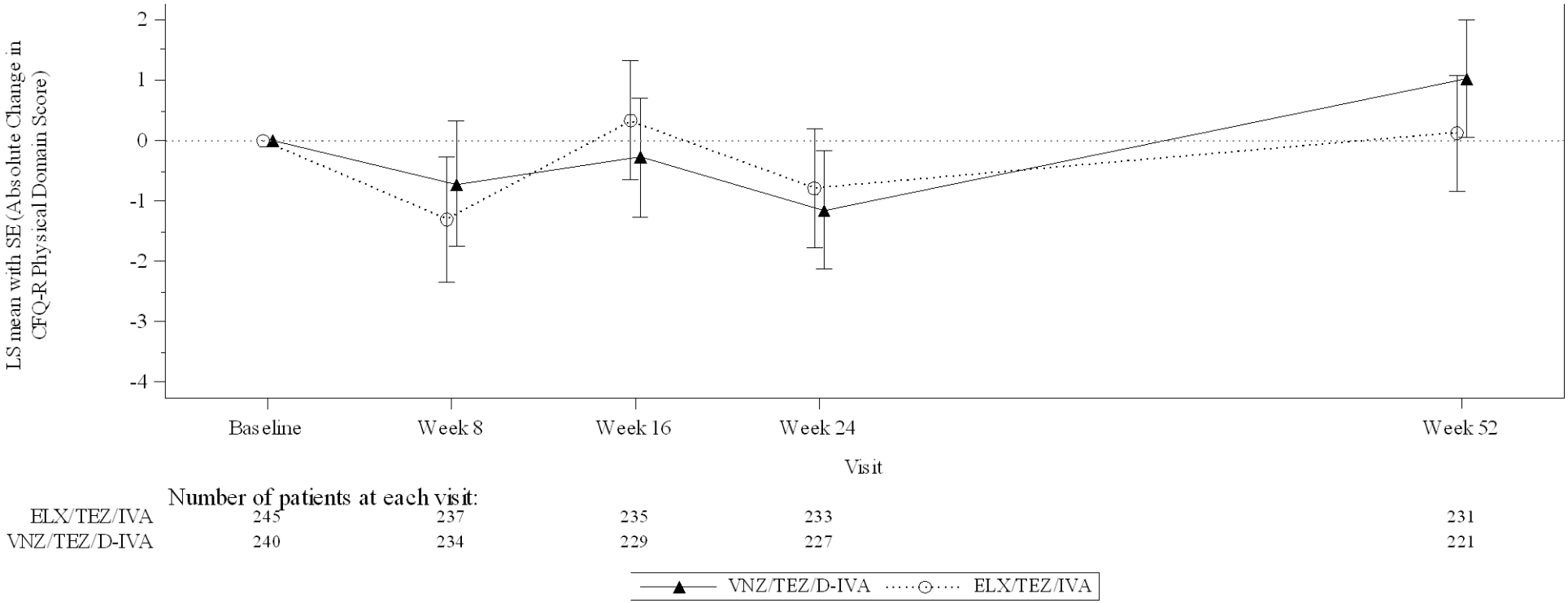
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years



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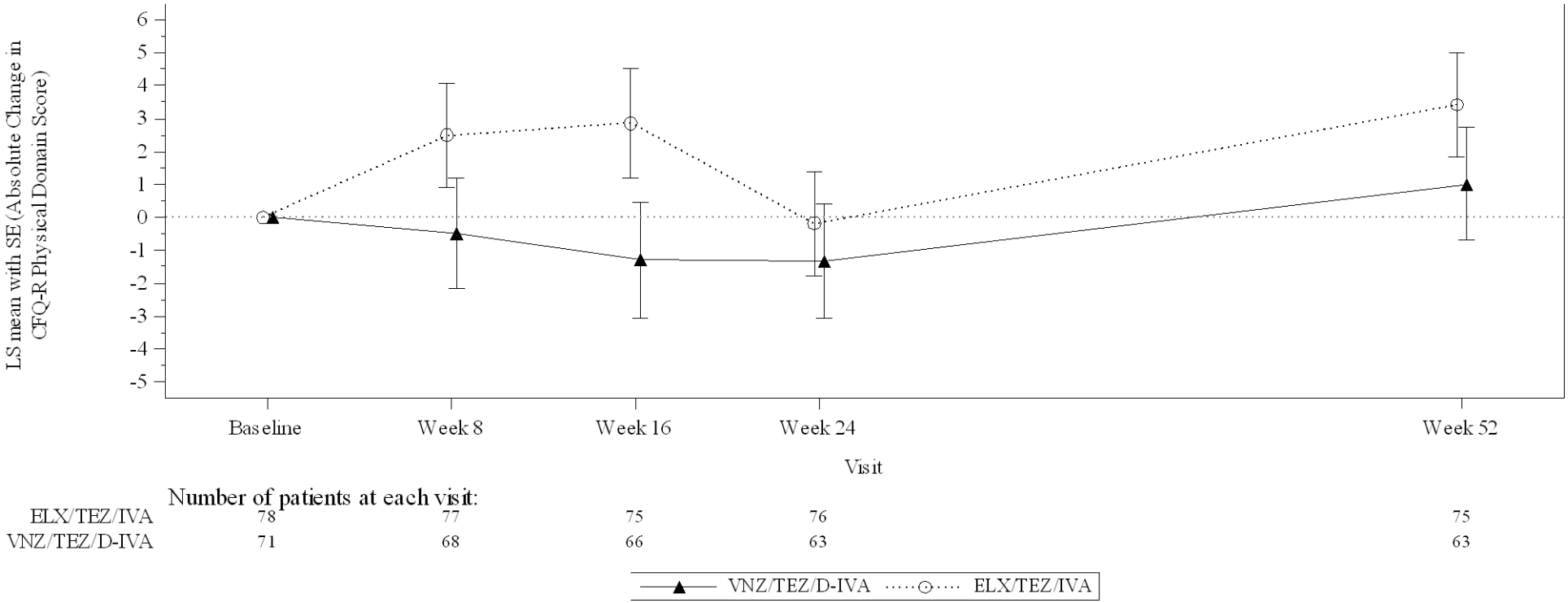
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L



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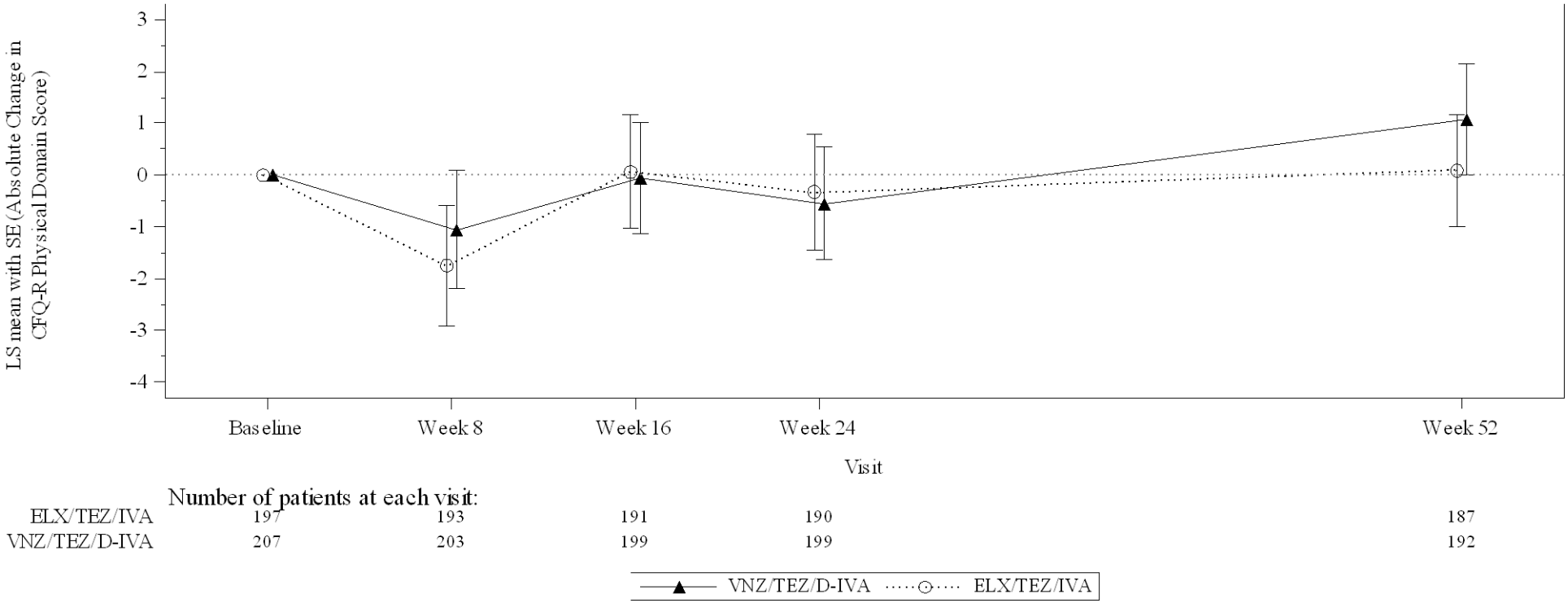
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L



Number of patients at each visit:

ELX/TEZ/IVA	197	193	191	190	187
VNZ/TEZ/D-IVA	207	203	199	199	192

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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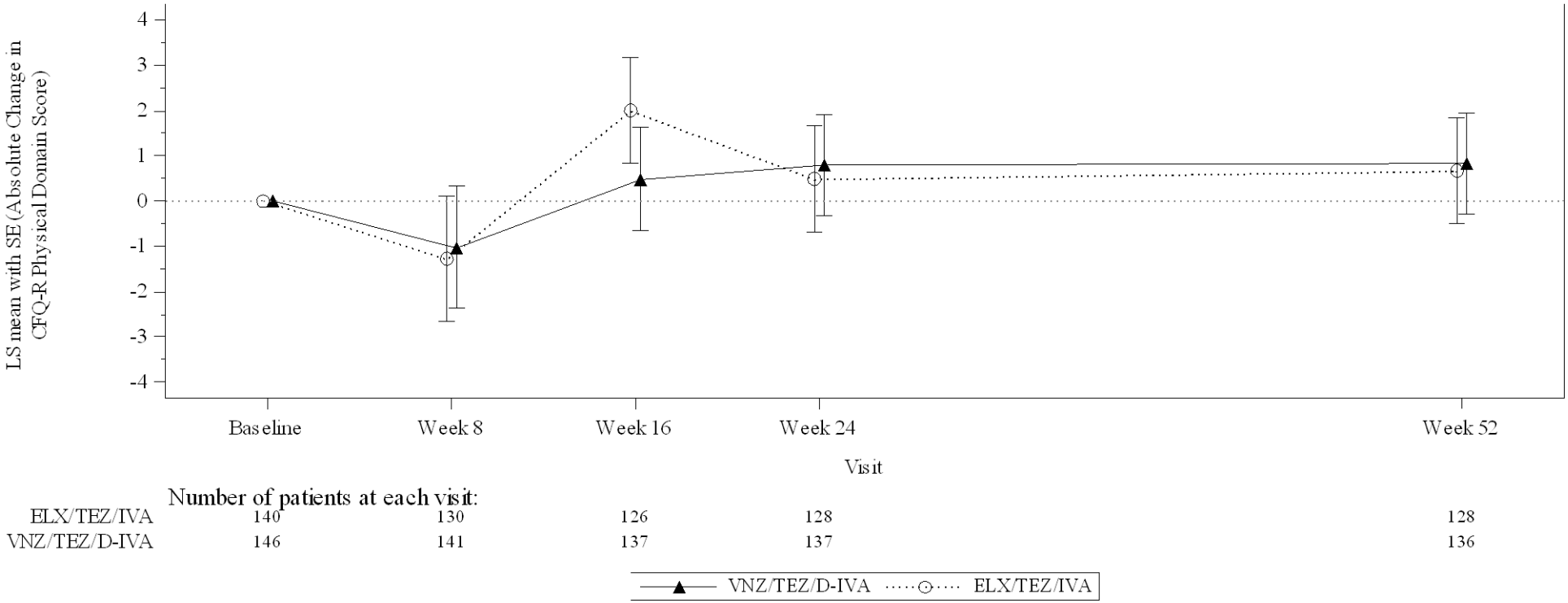
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male



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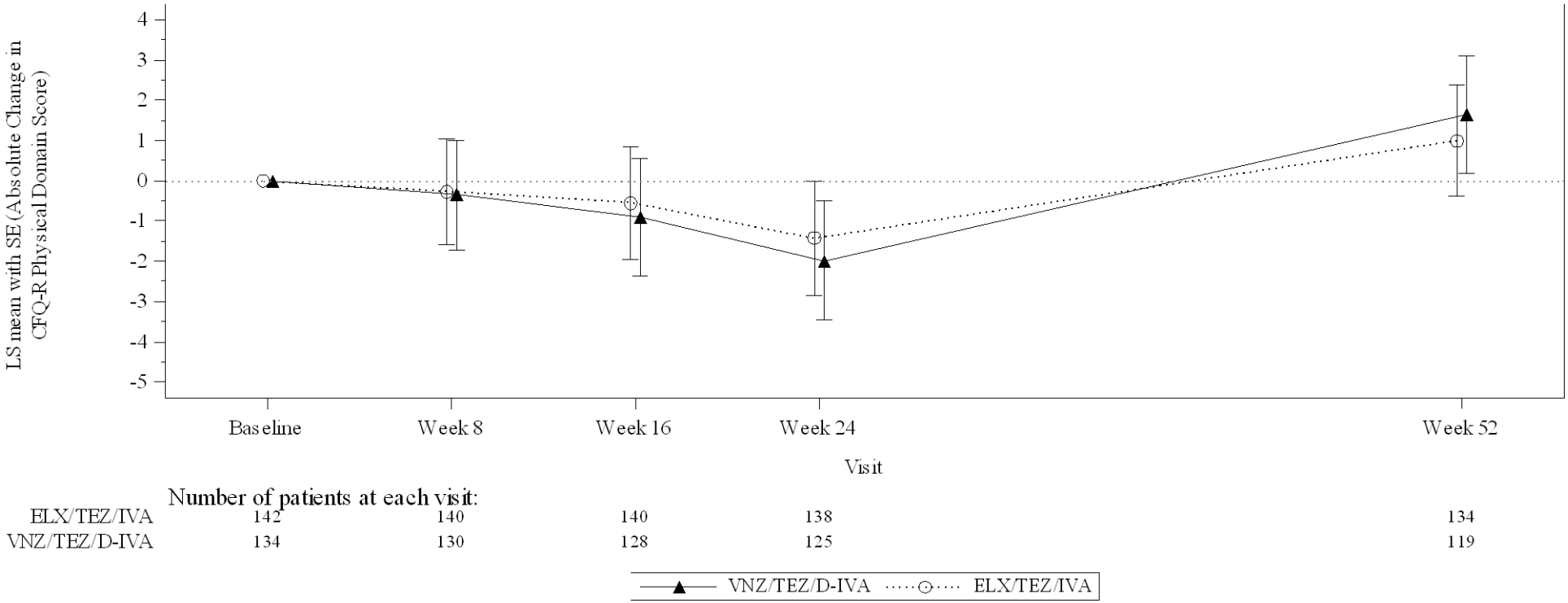
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female



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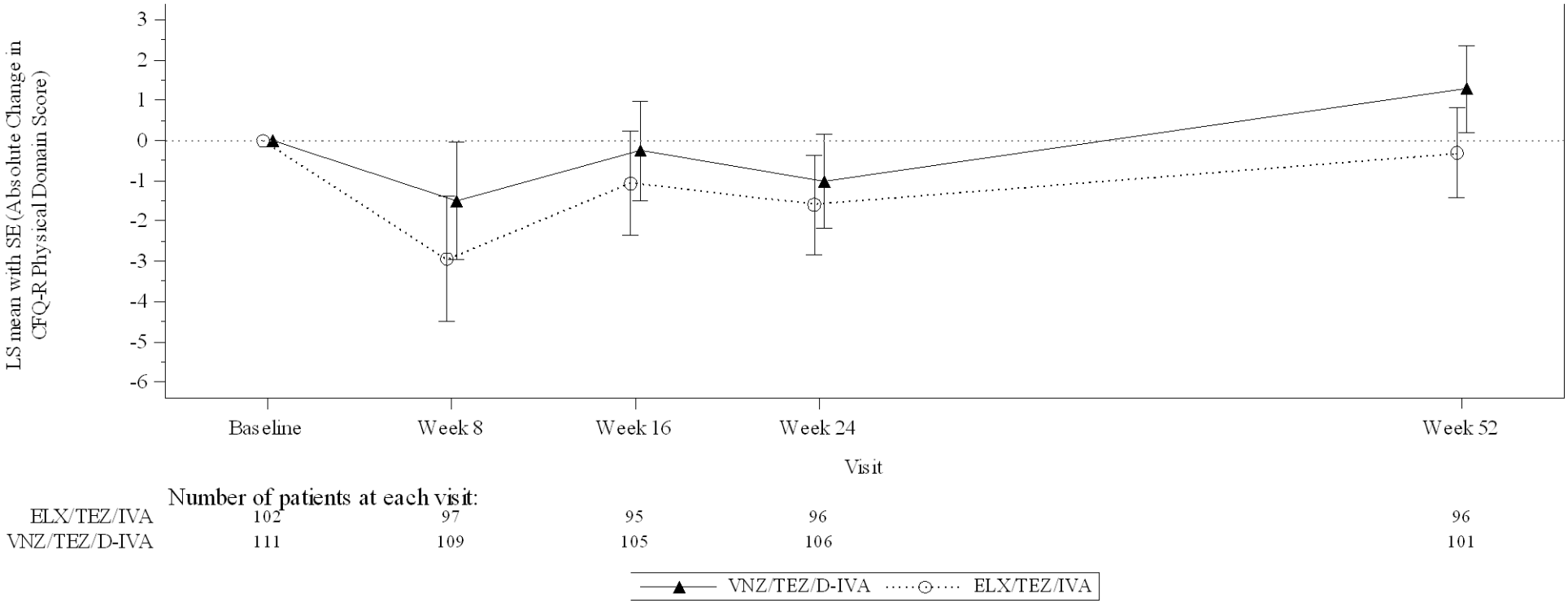
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America



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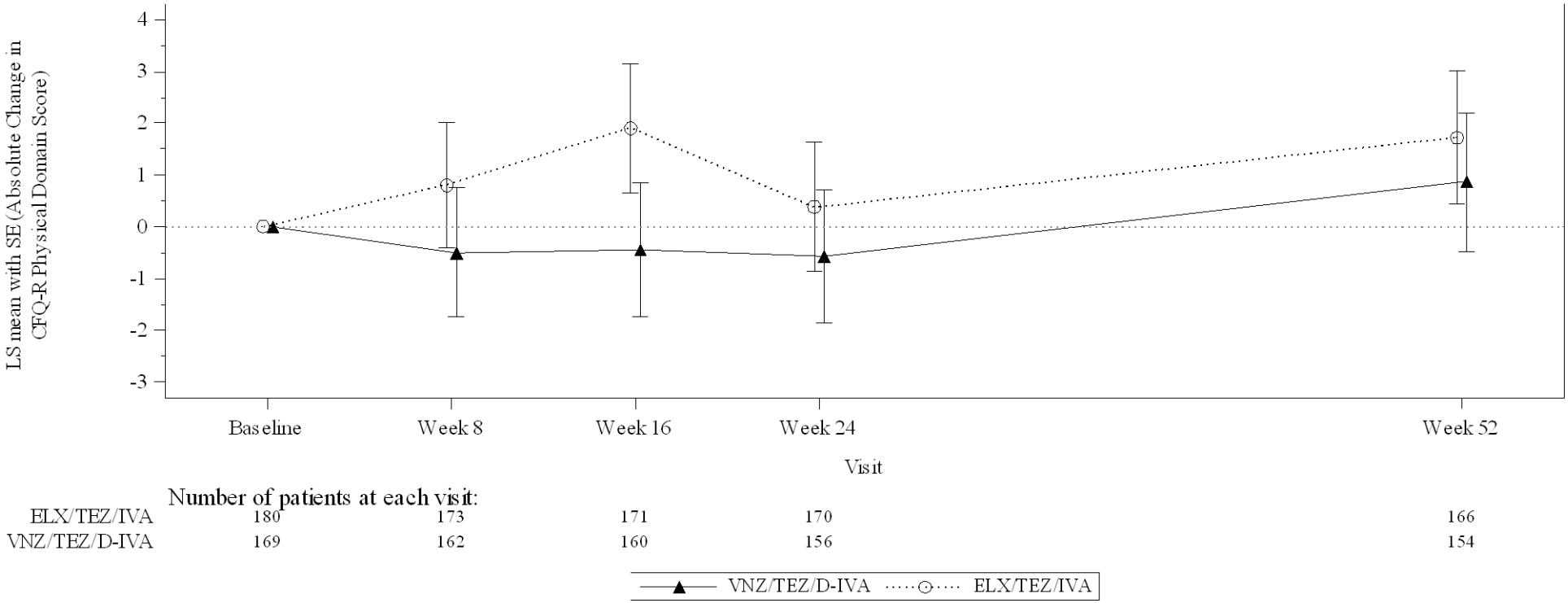
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World



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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
ppFEV$_1$ at baseline <70 %

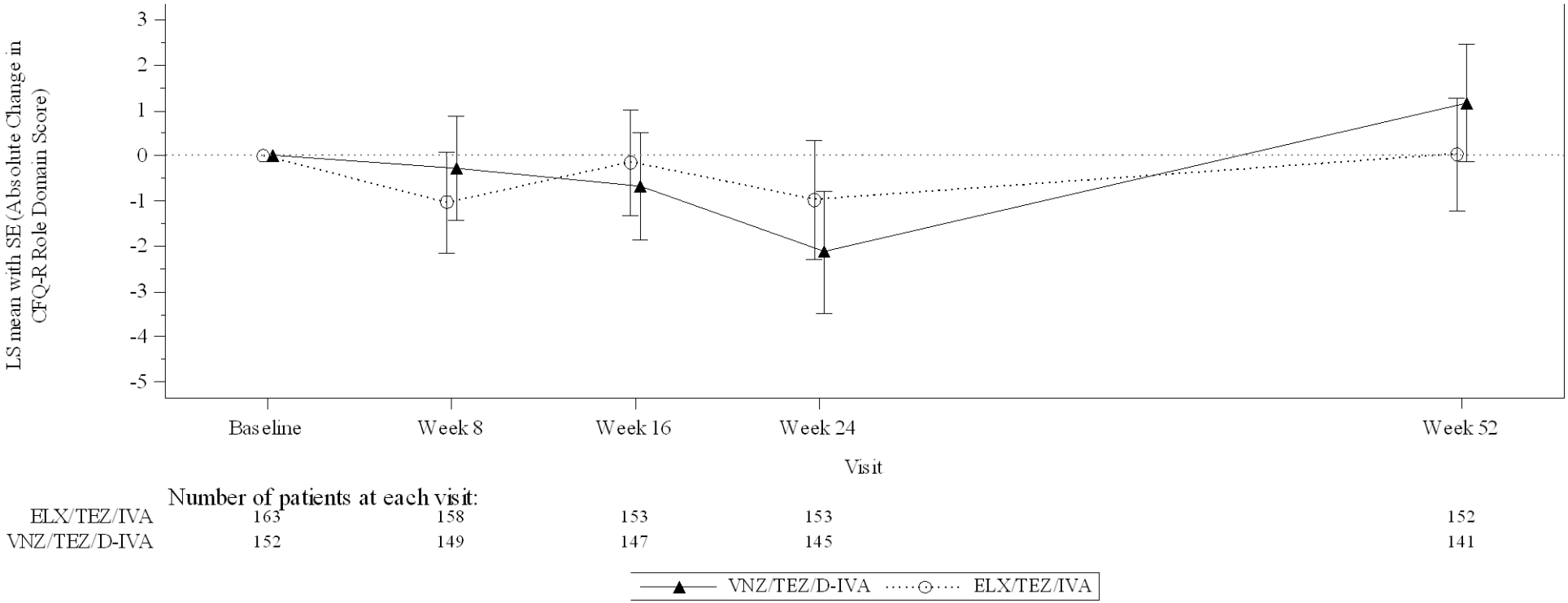

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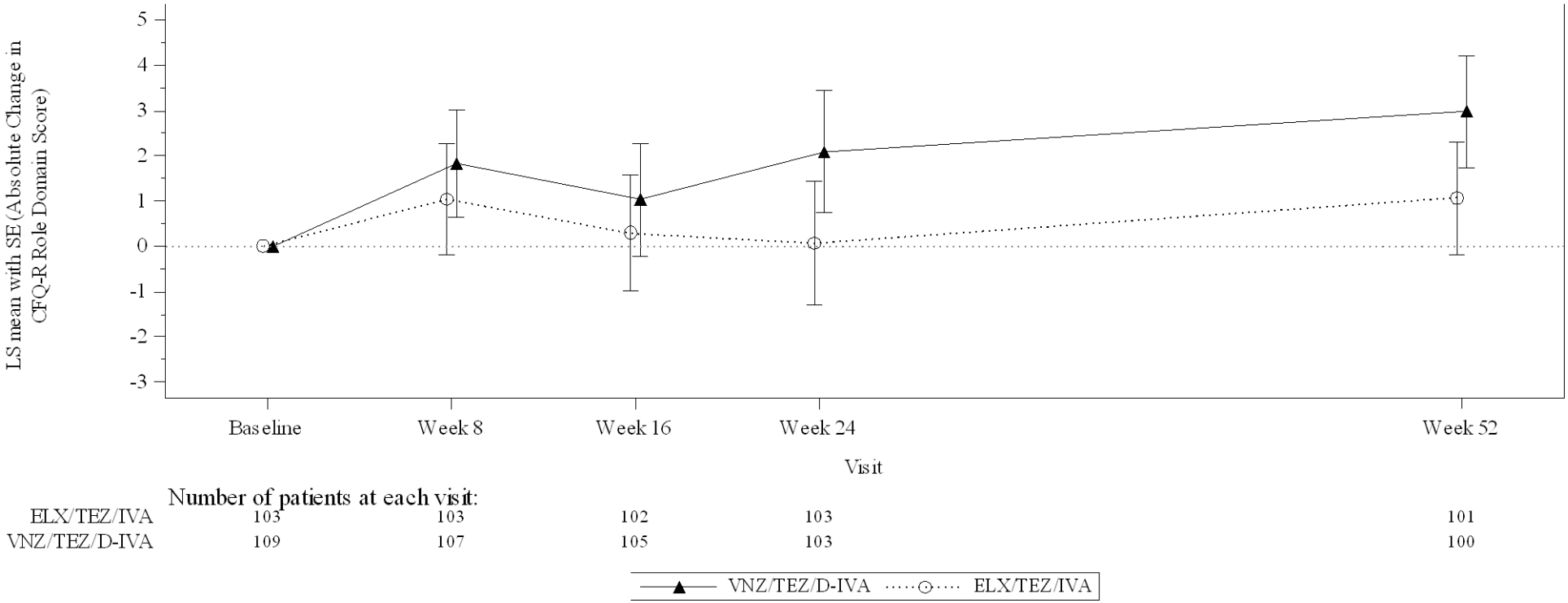
Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
ppFEV$_1$ at baseline ≥70 %



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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years

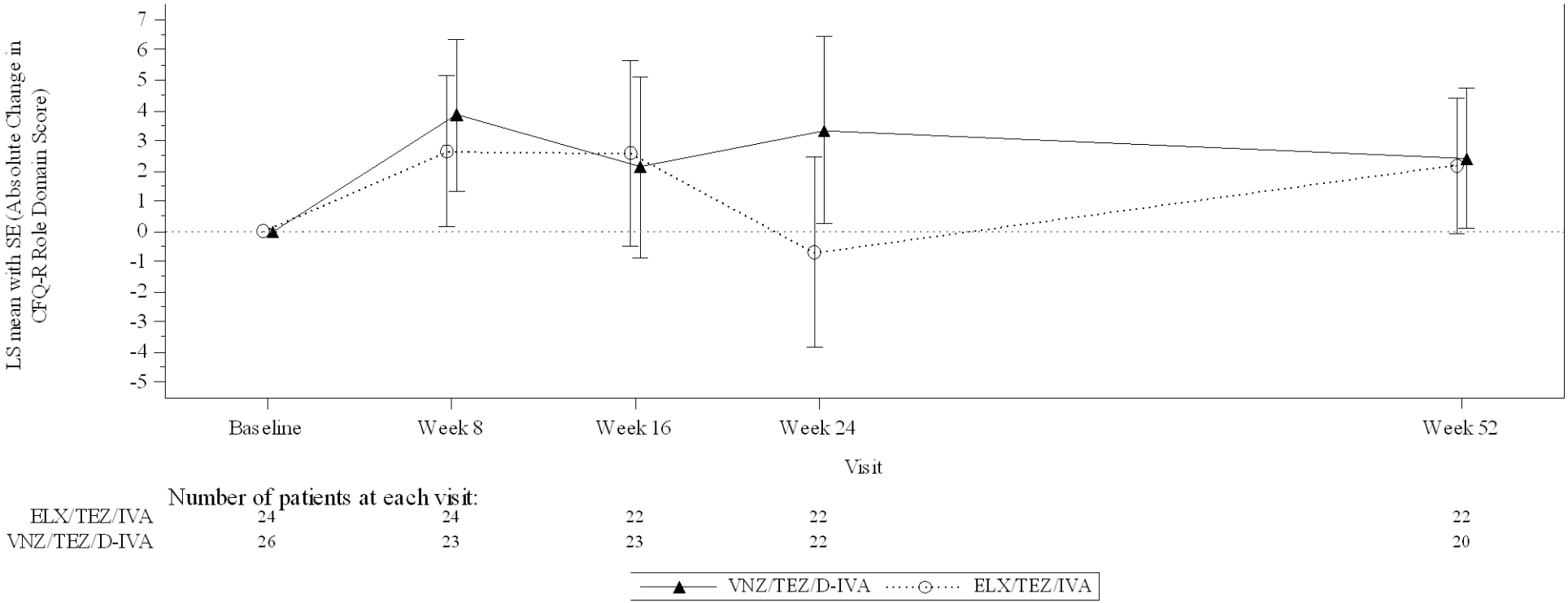

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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years

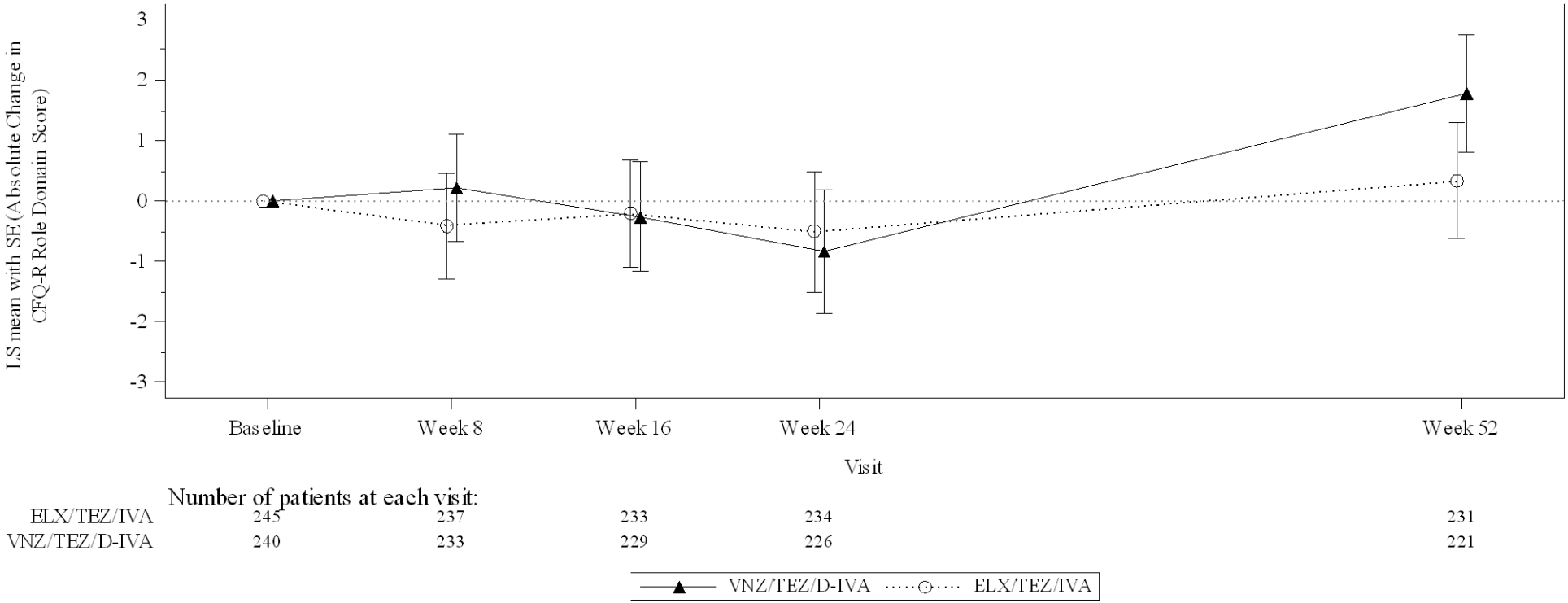

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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L

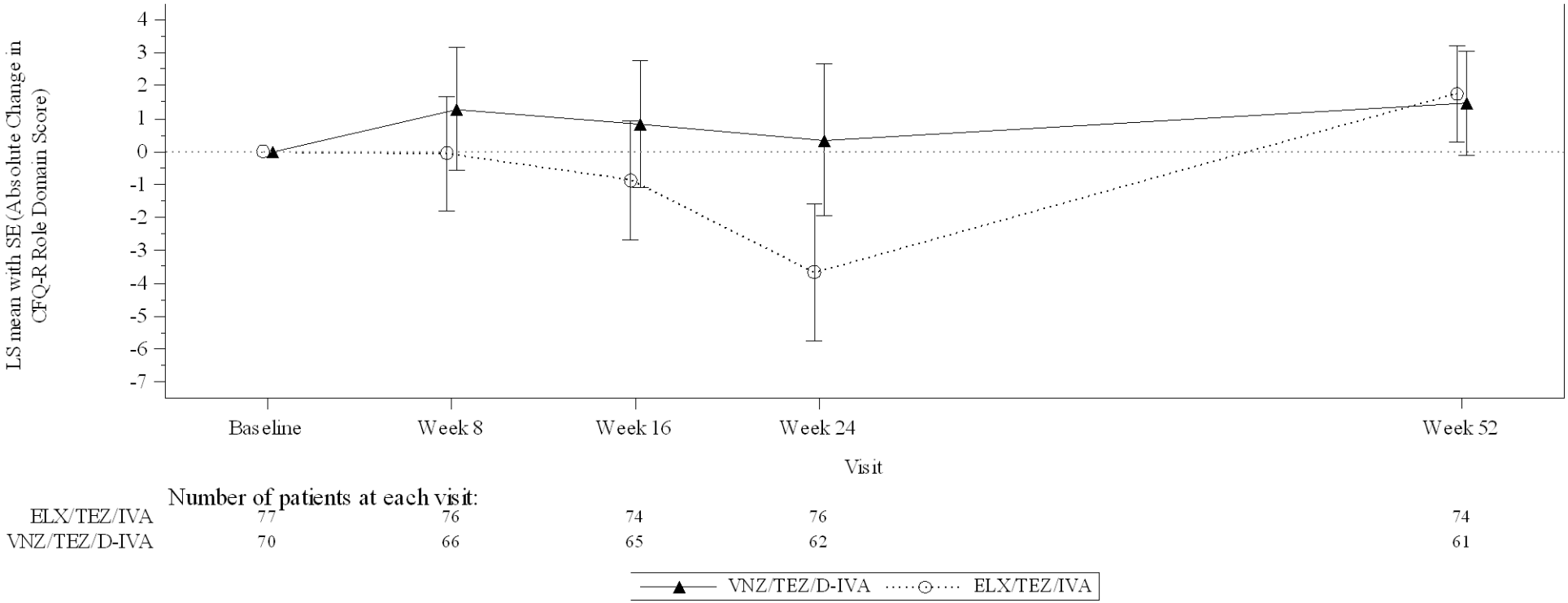

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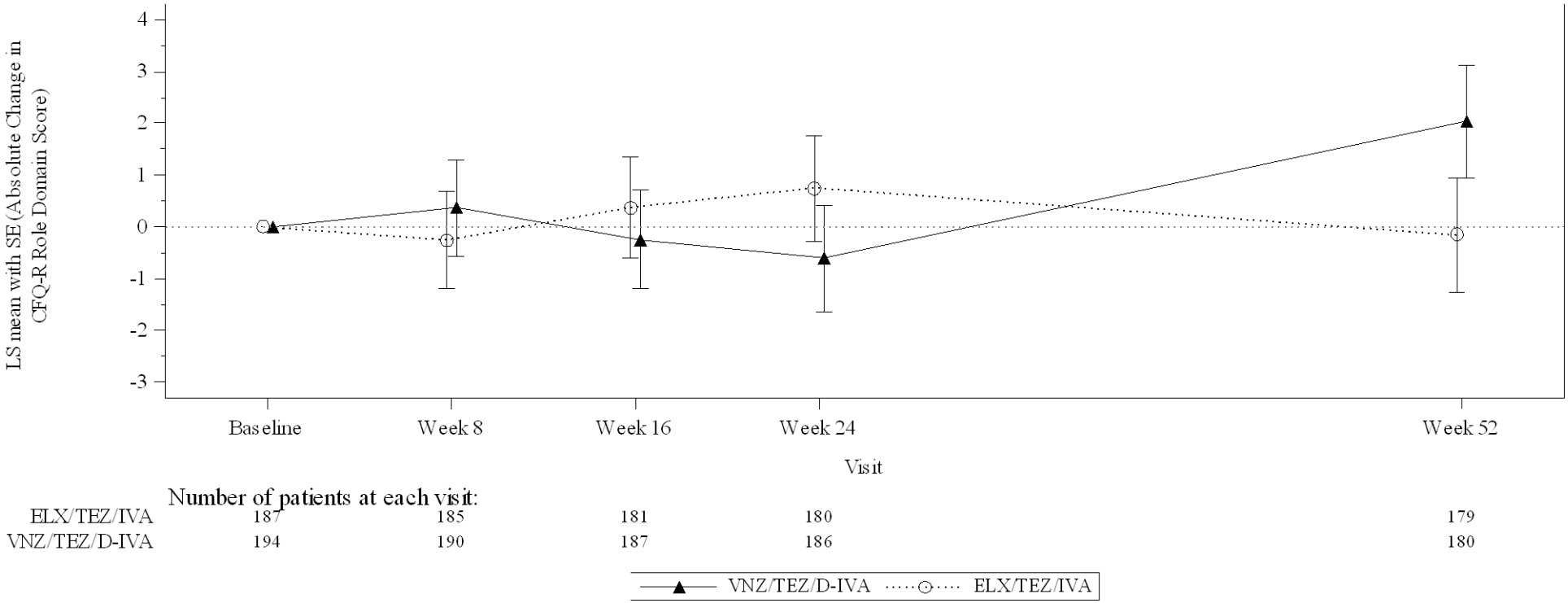
Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L



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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Male

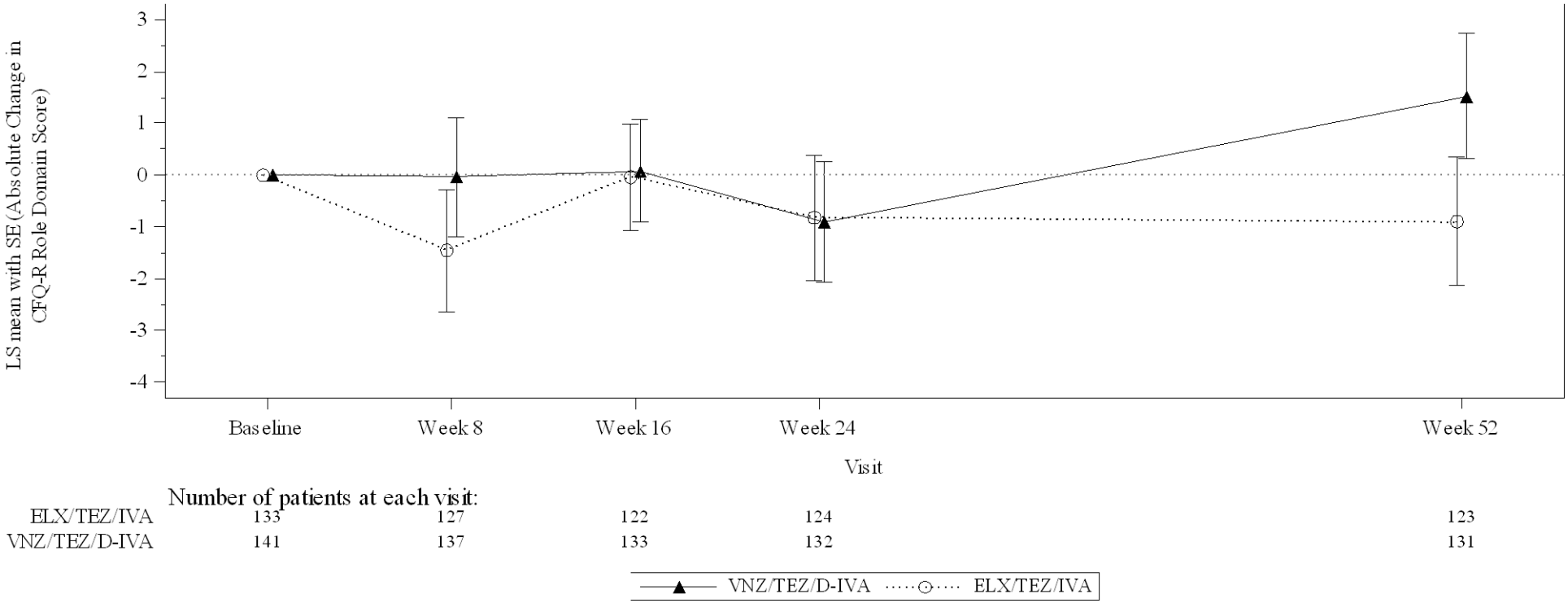

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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Female

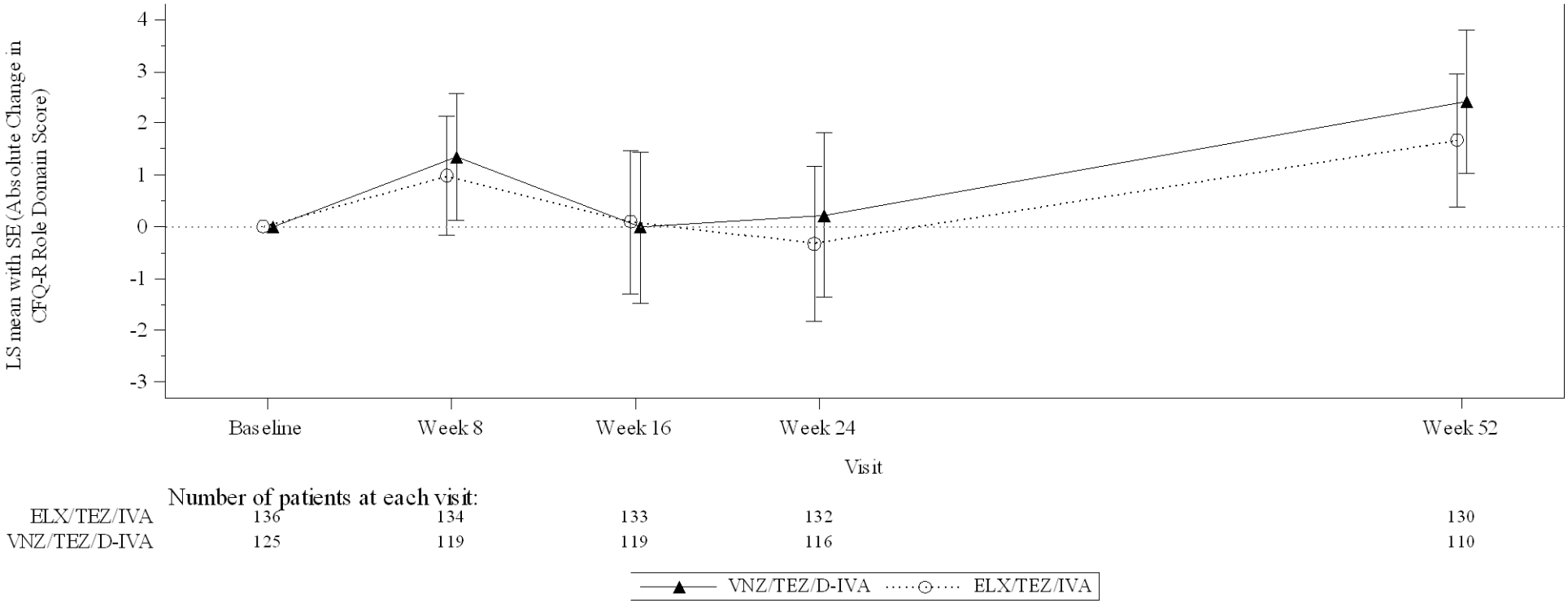

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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = North America

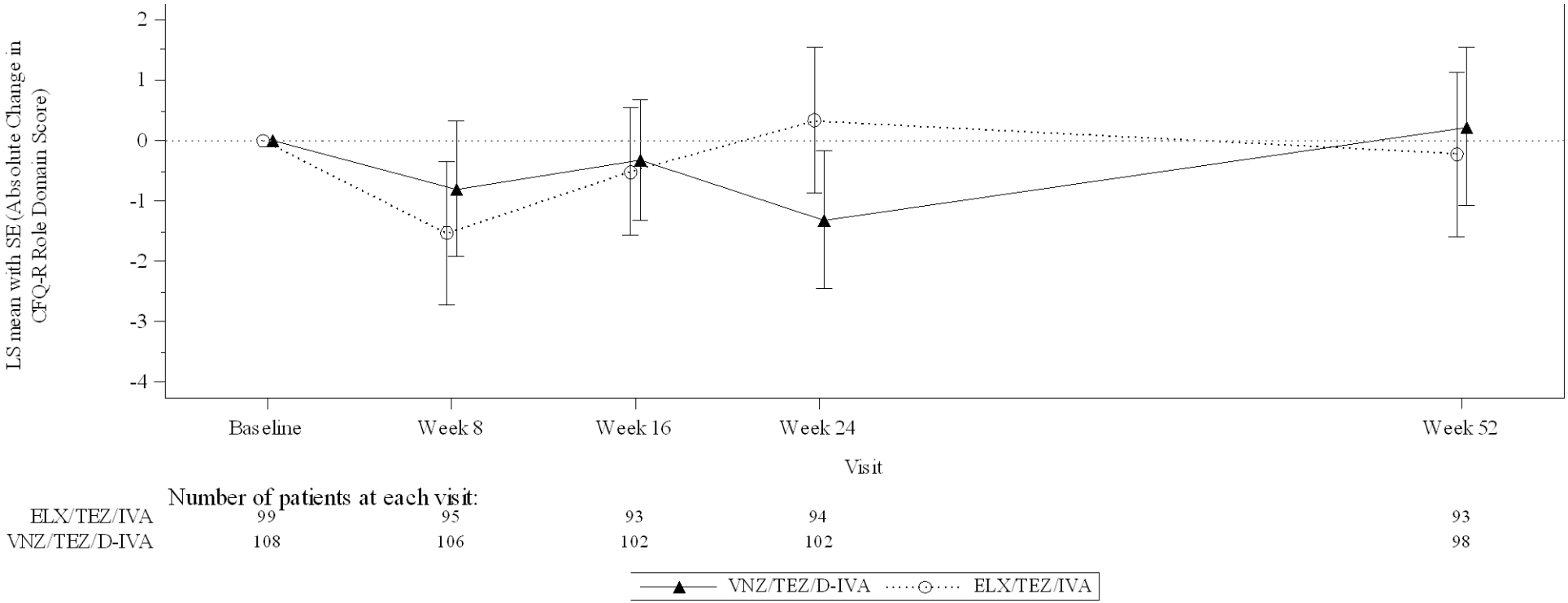

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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World

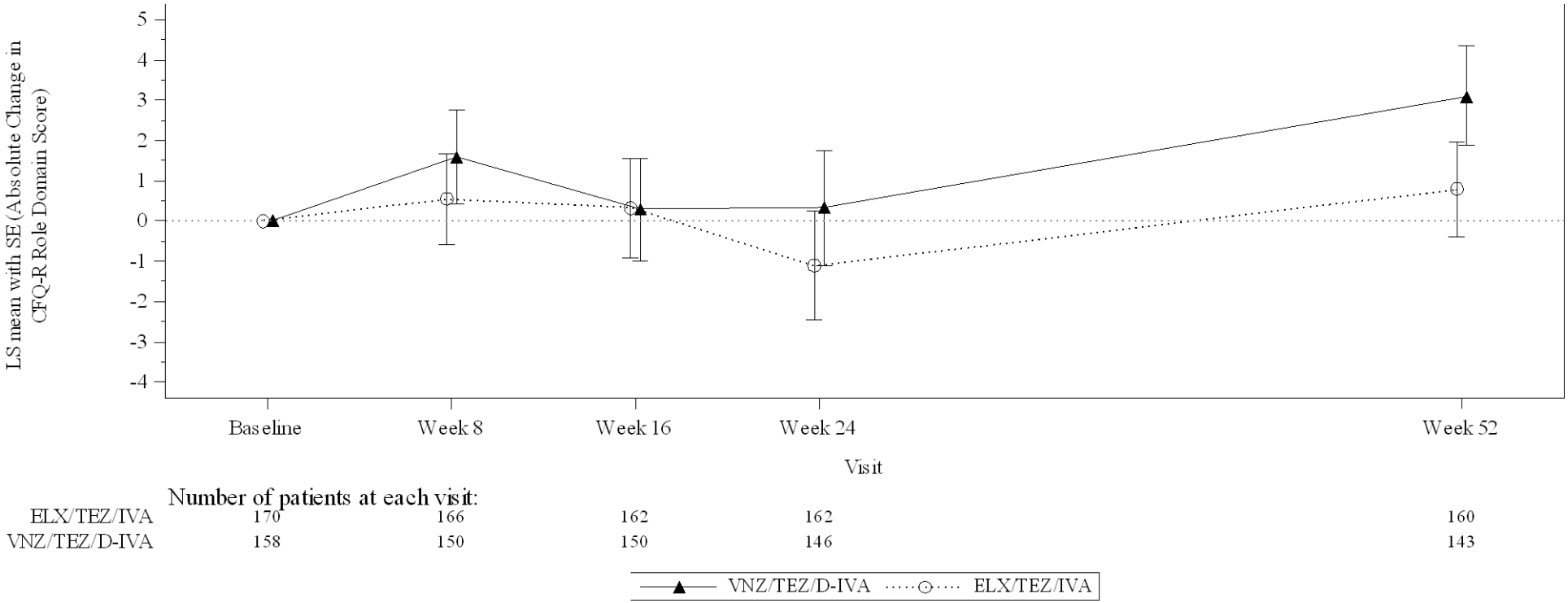

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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
ppFEV$_1$ at baseline <70 %

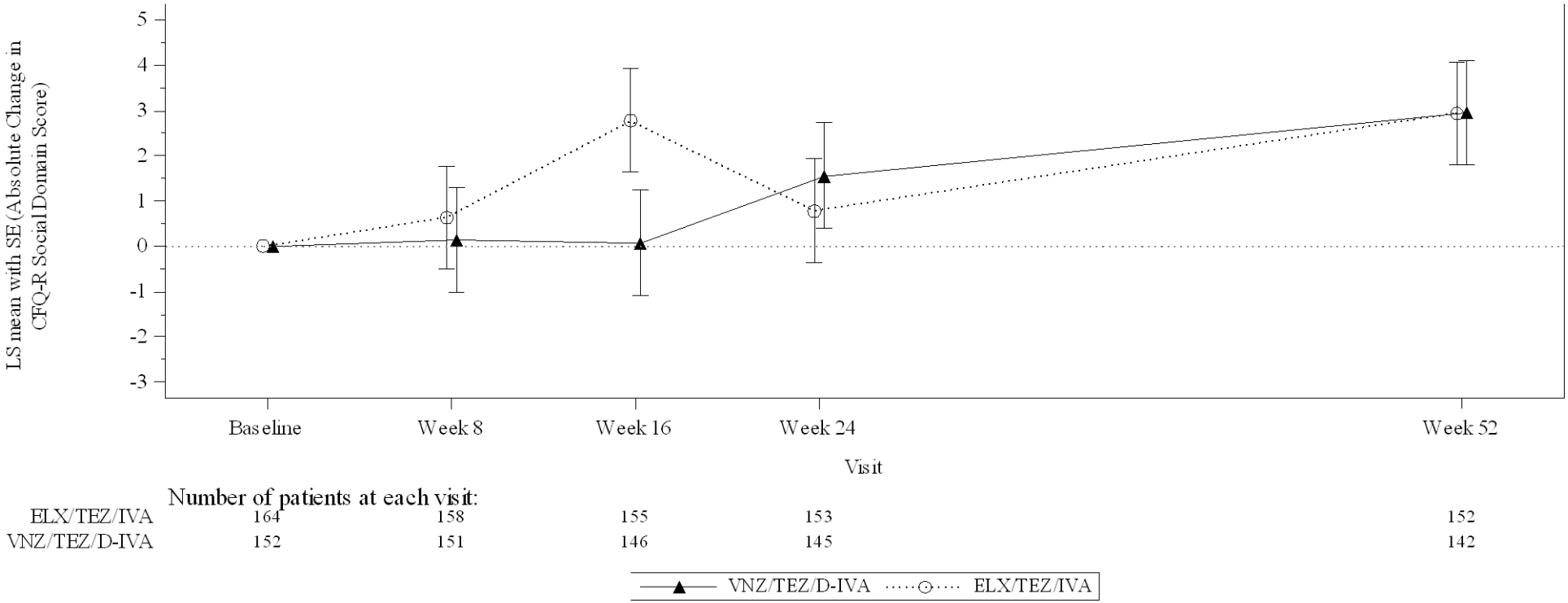

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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
ppFEV$_1$ at baseline ≥70 %

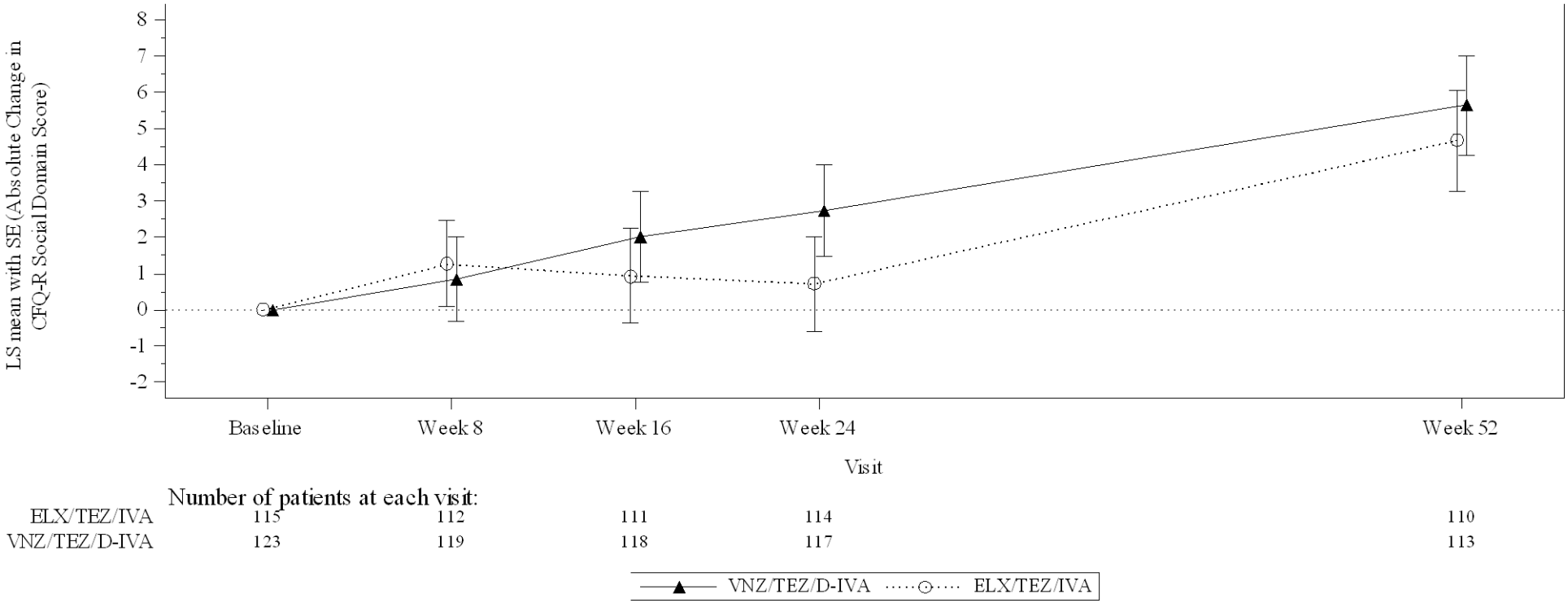

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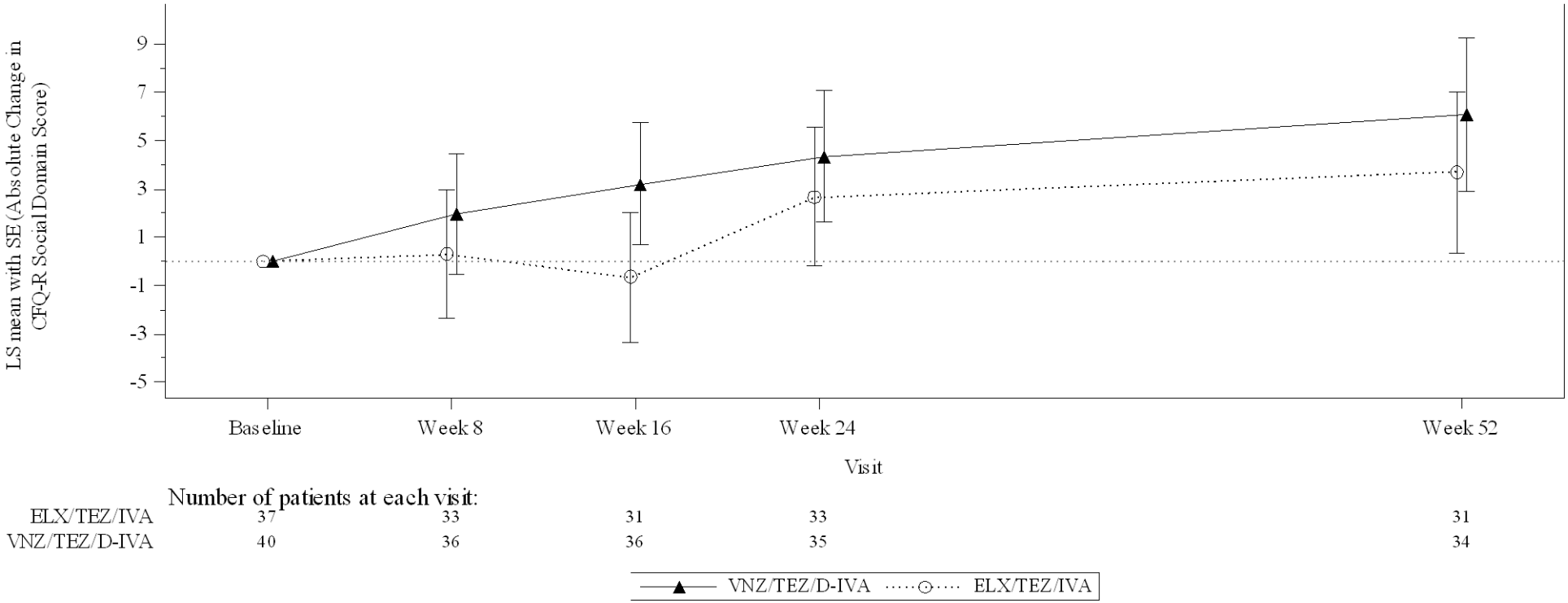
Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years



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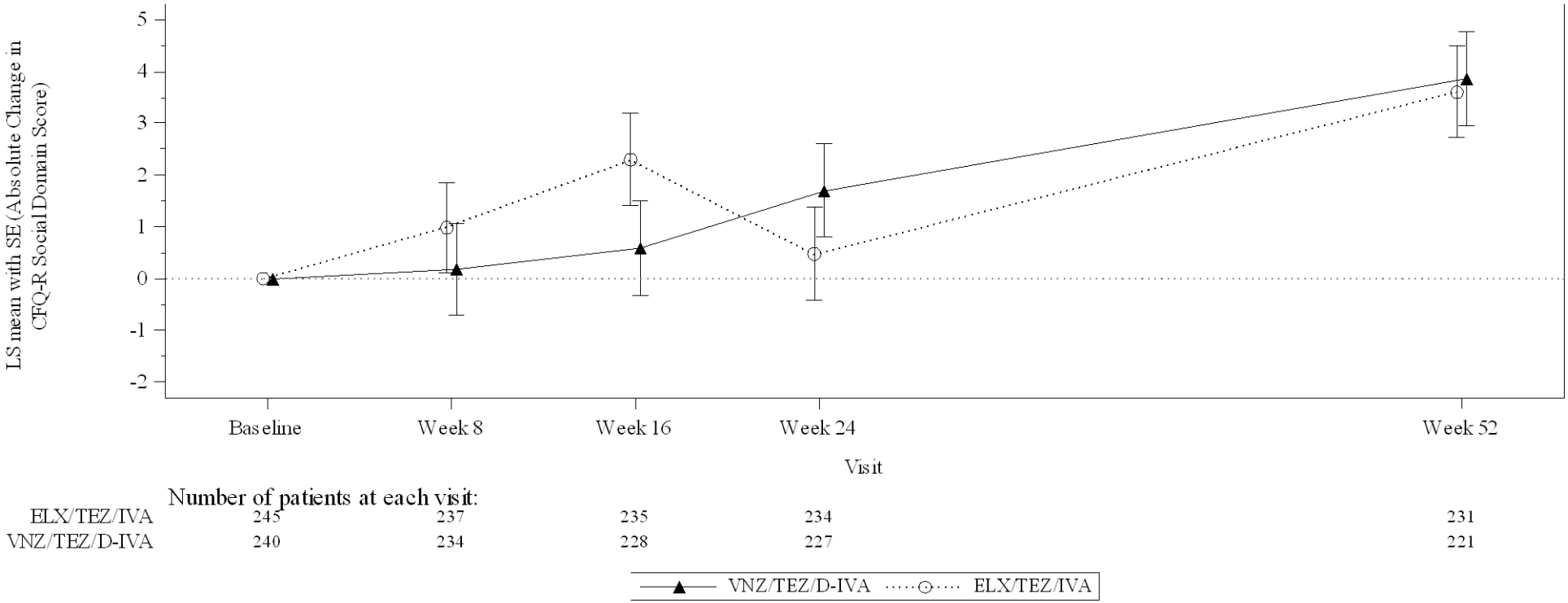
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years



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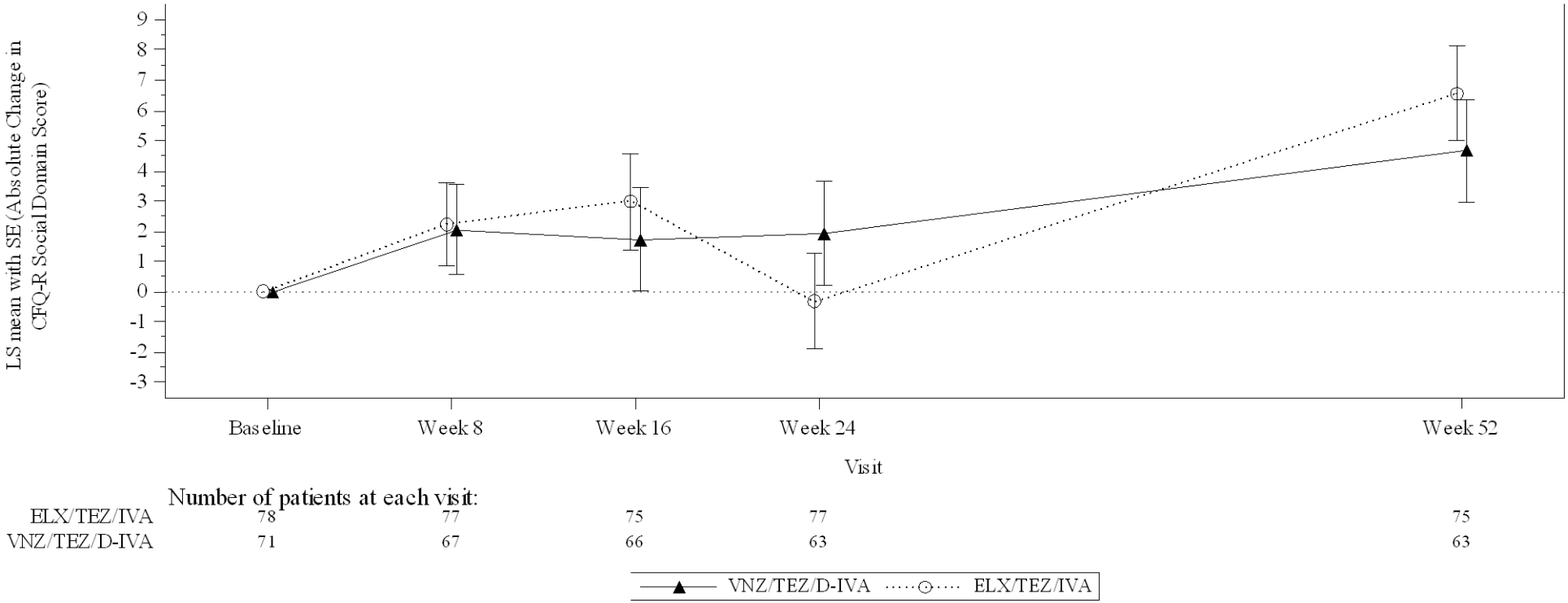
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L



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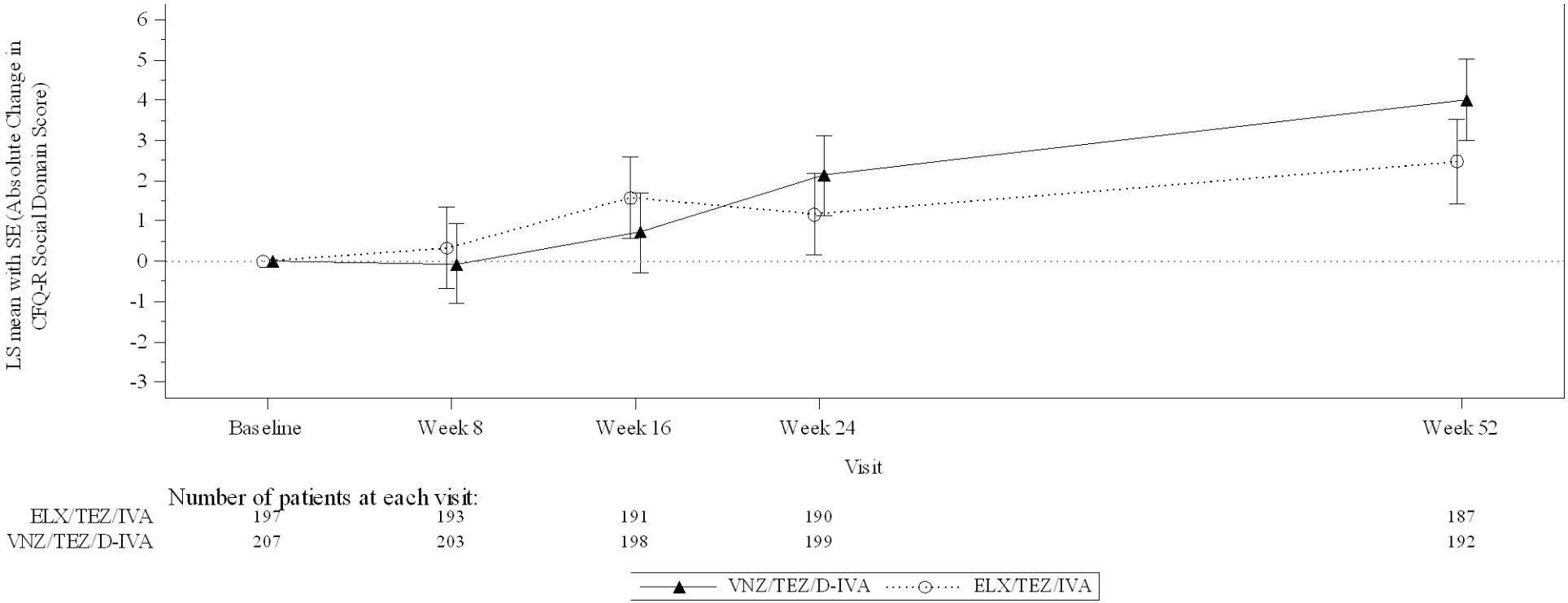
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L



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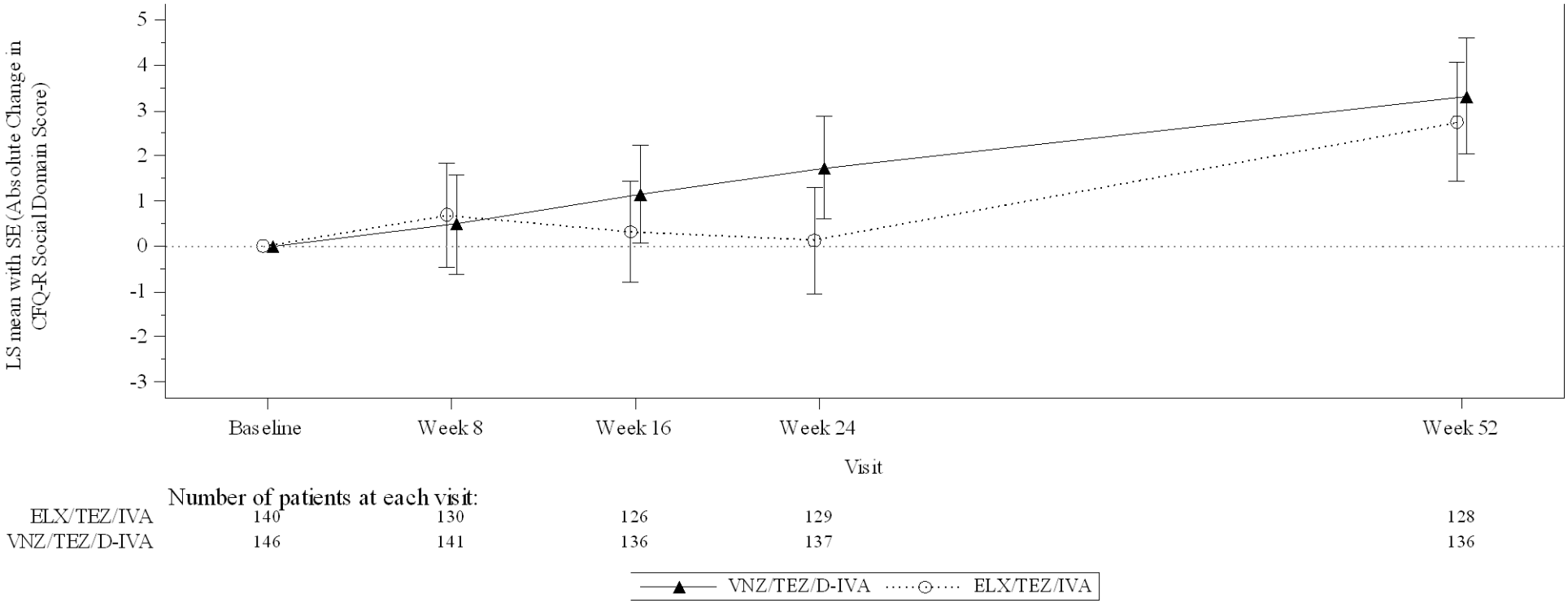
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male



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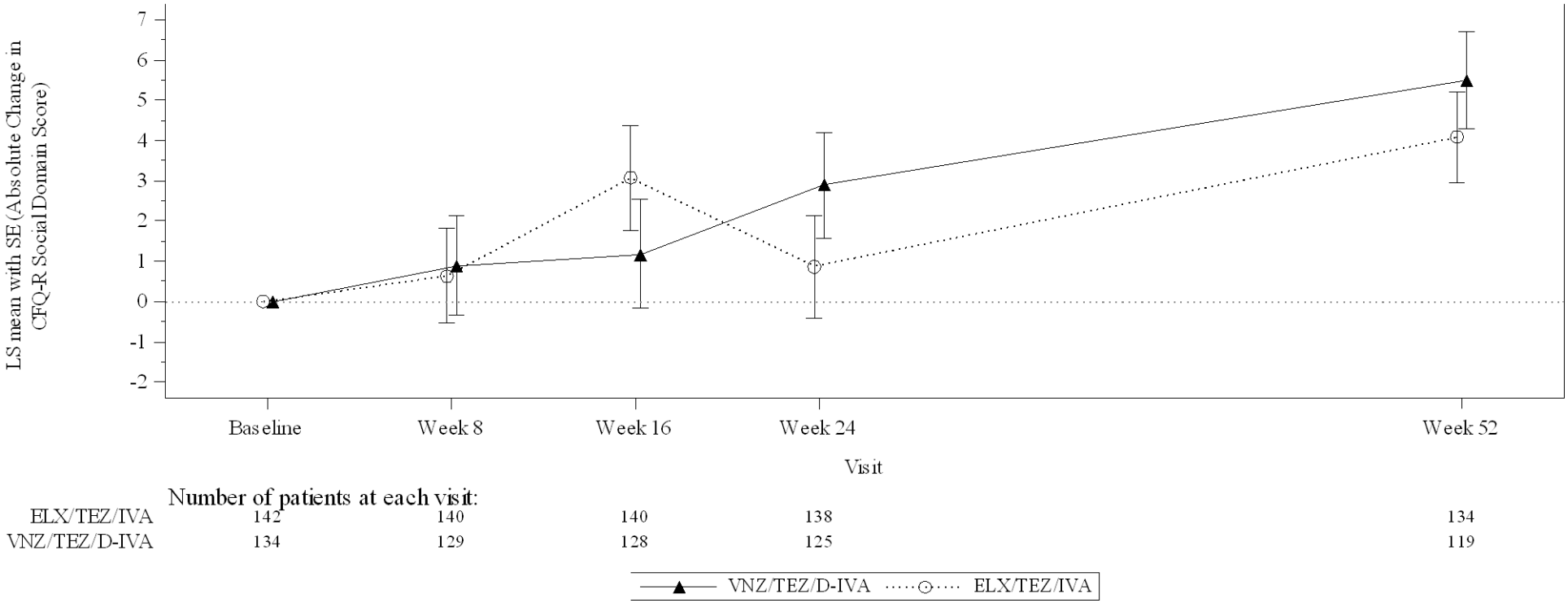
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female



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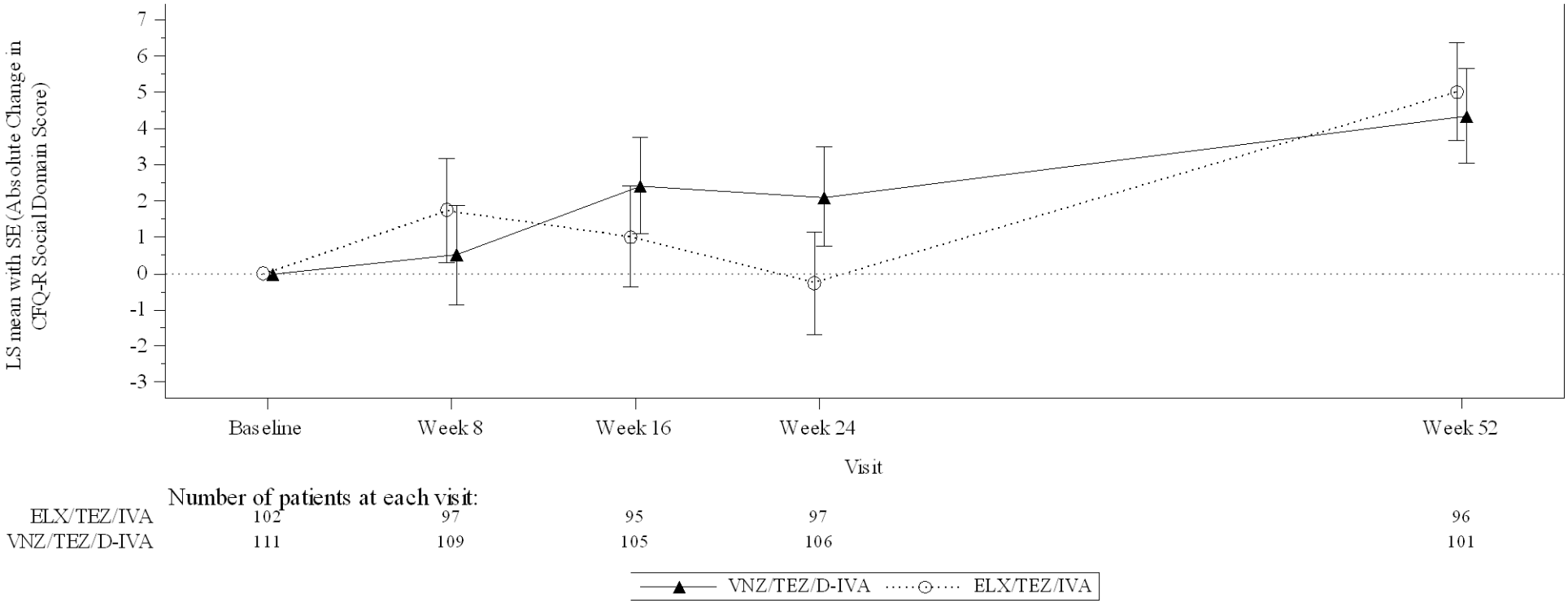
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America



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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

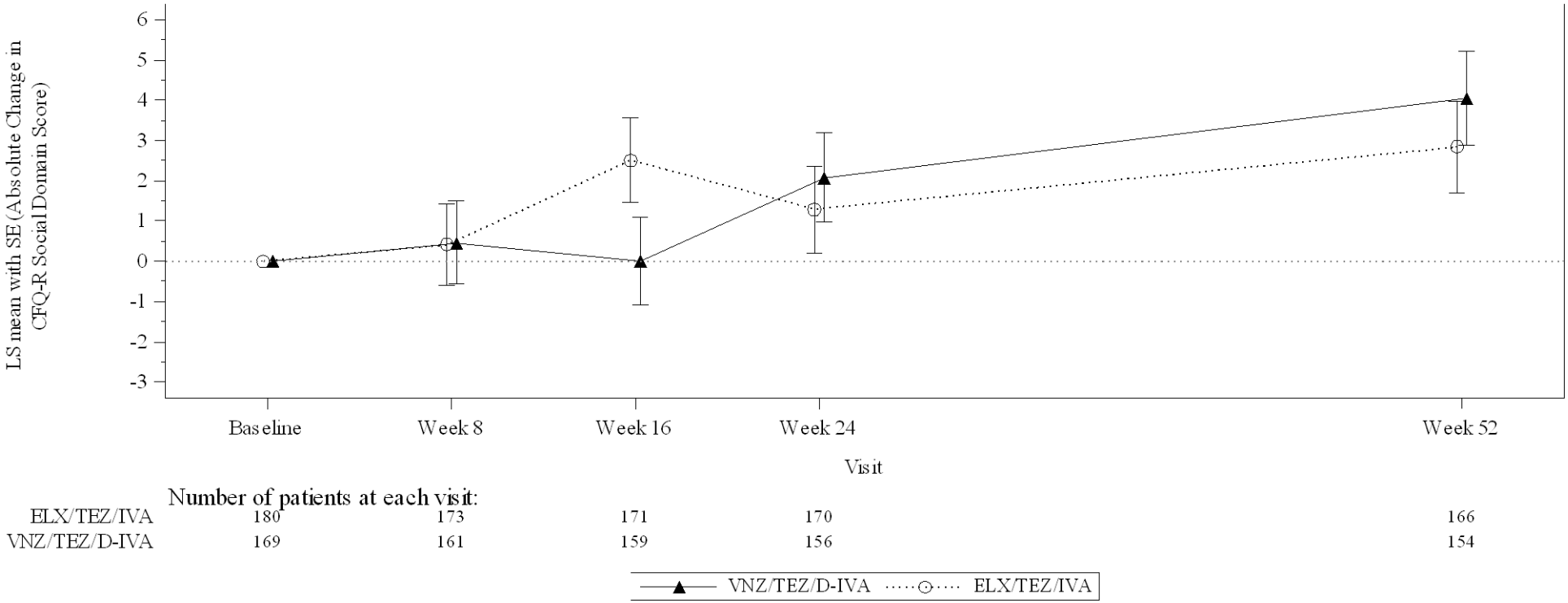

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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
ppFEV$_1$ at baseline <70 %

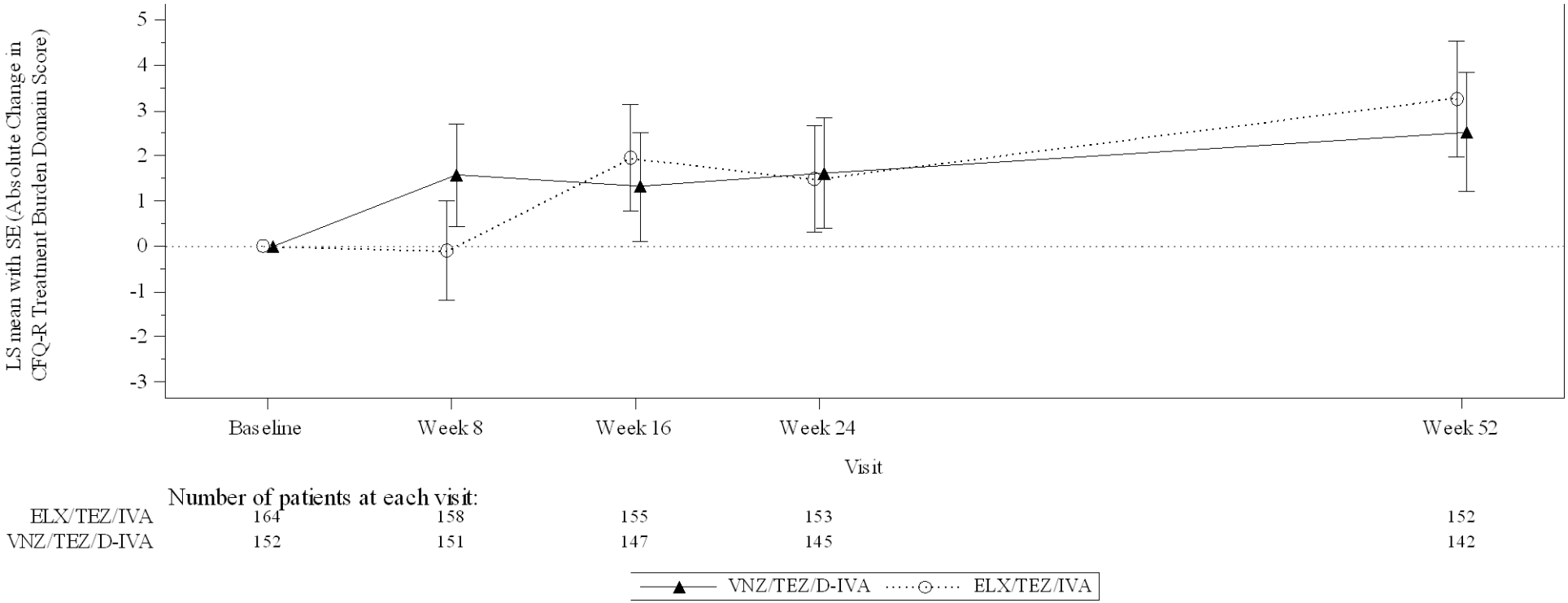

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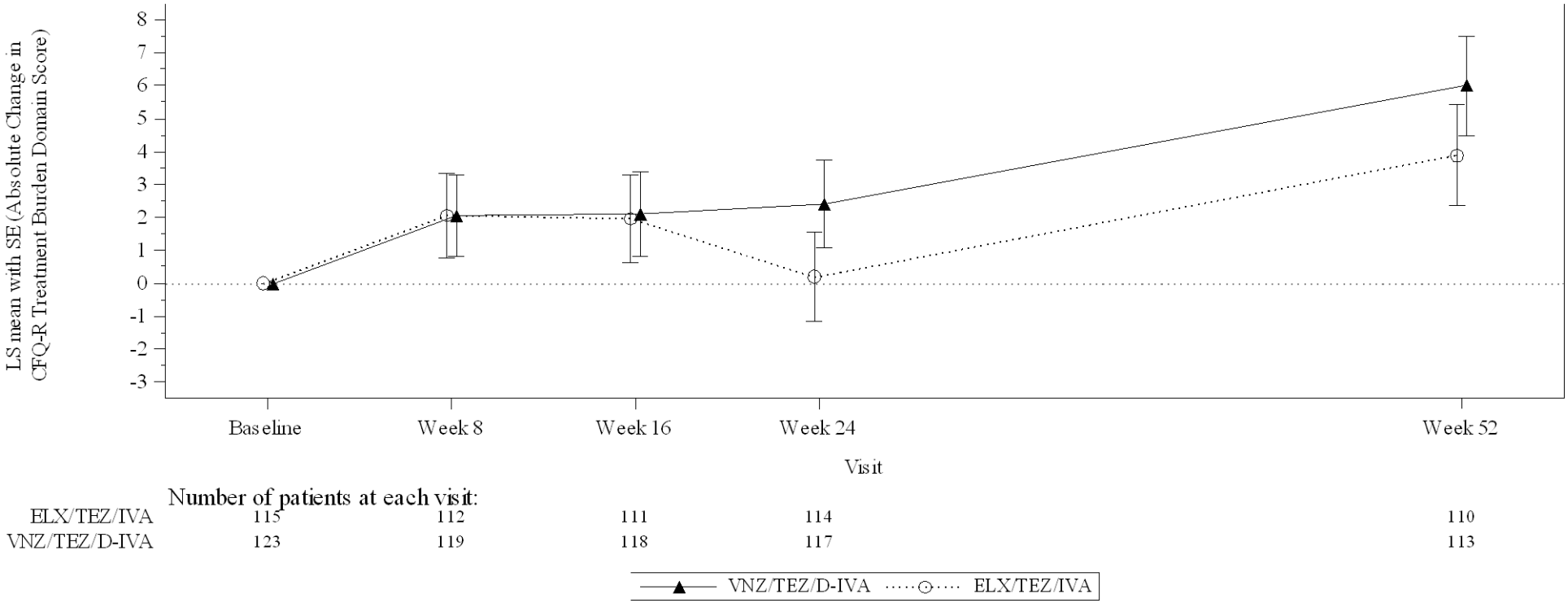
Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
ppFEV$_1$ at baseline ≥70 %



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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

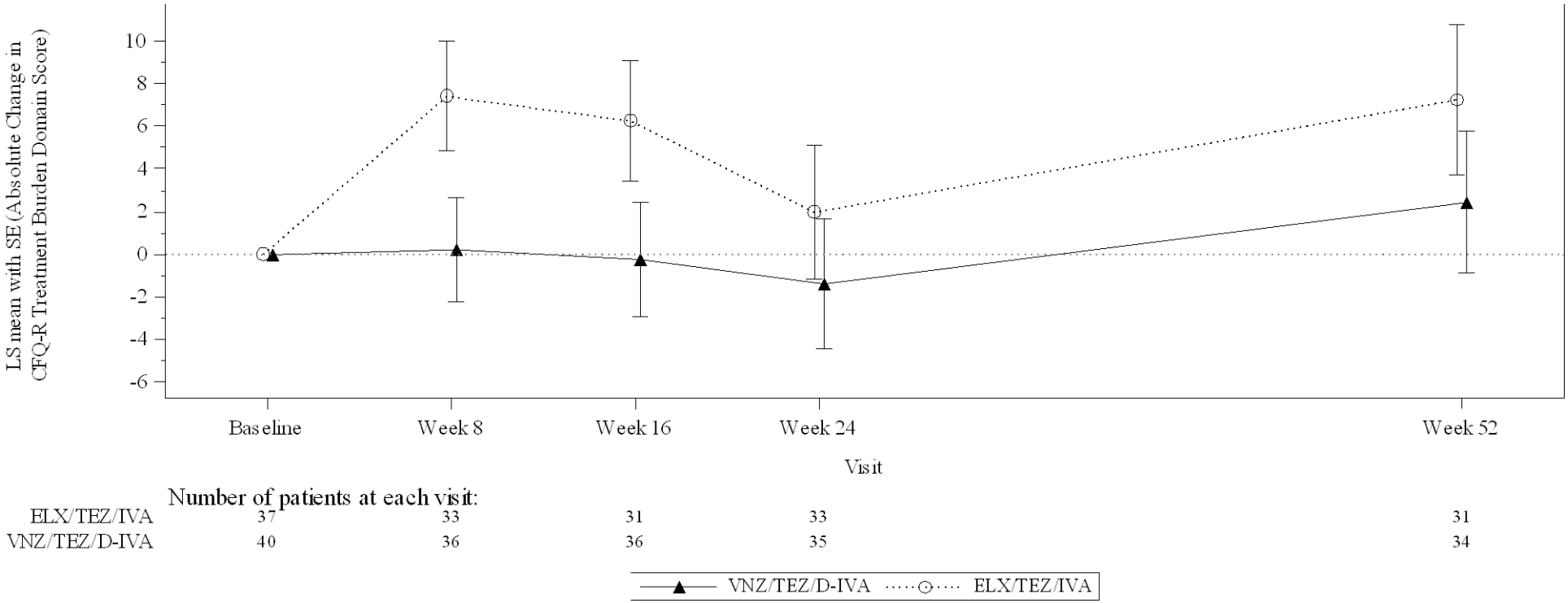

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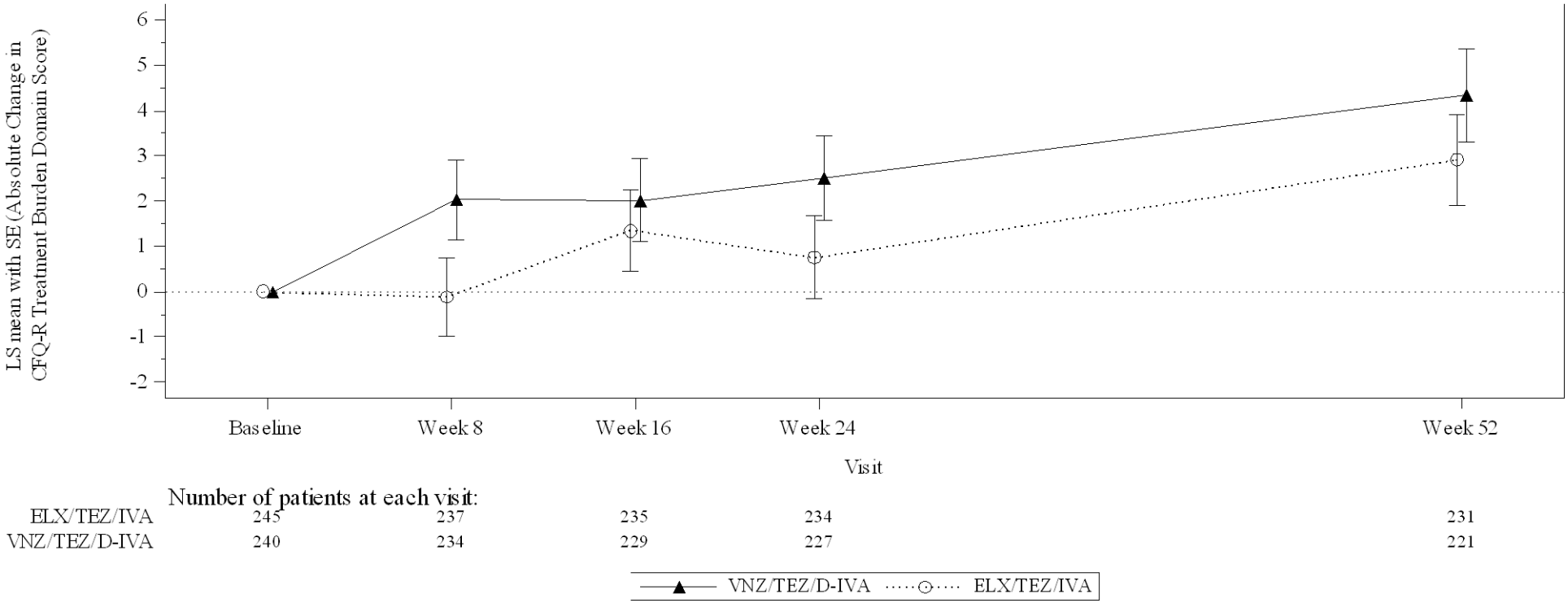
Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years



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Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

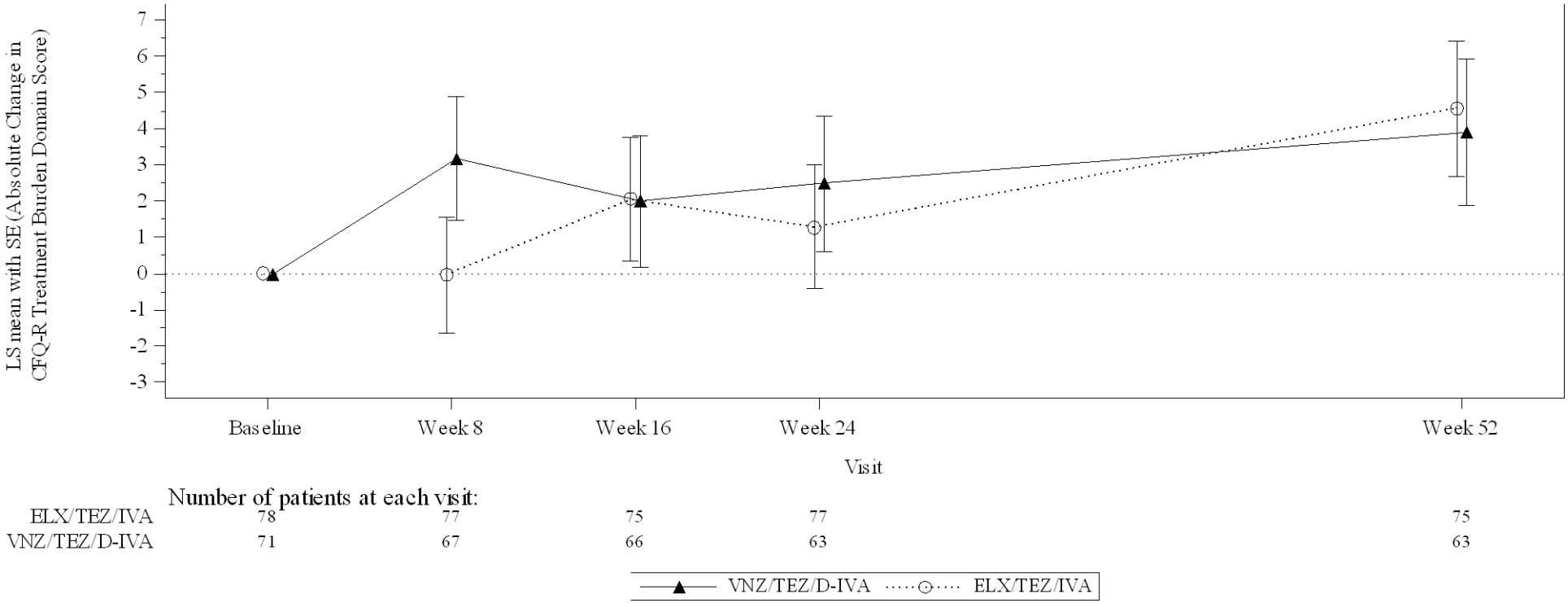

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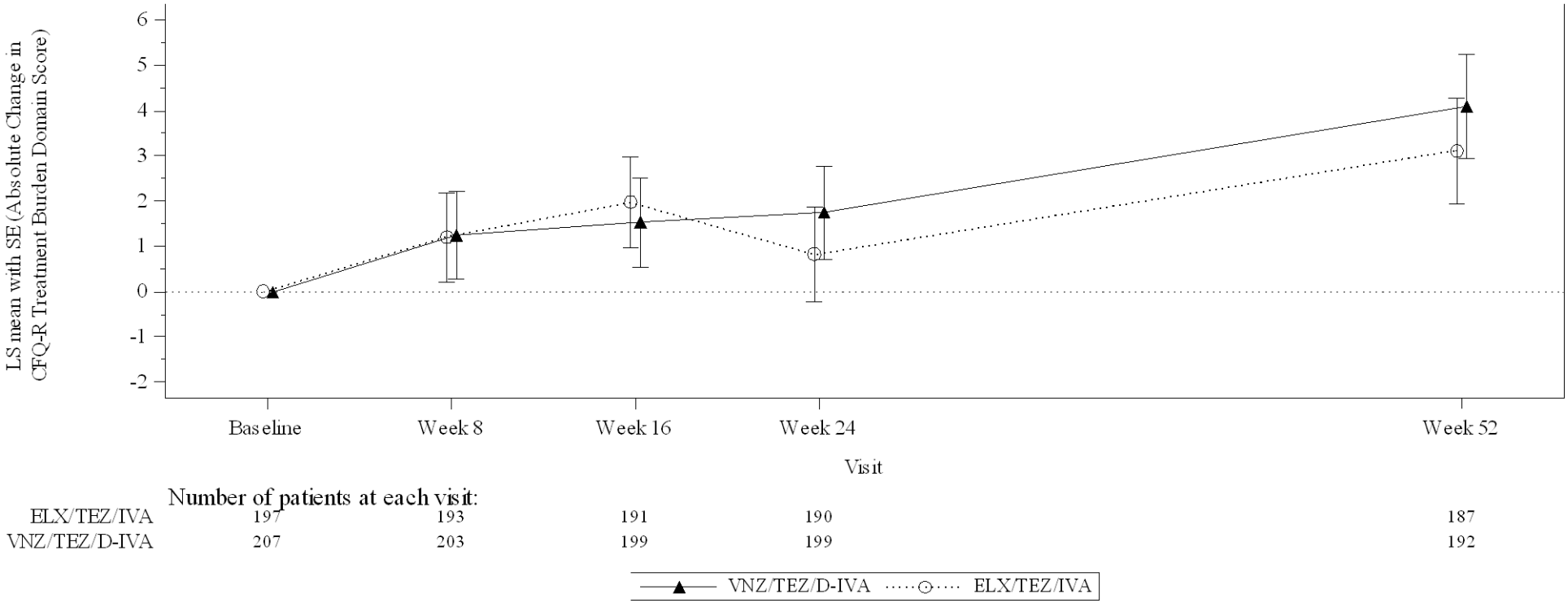
Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L



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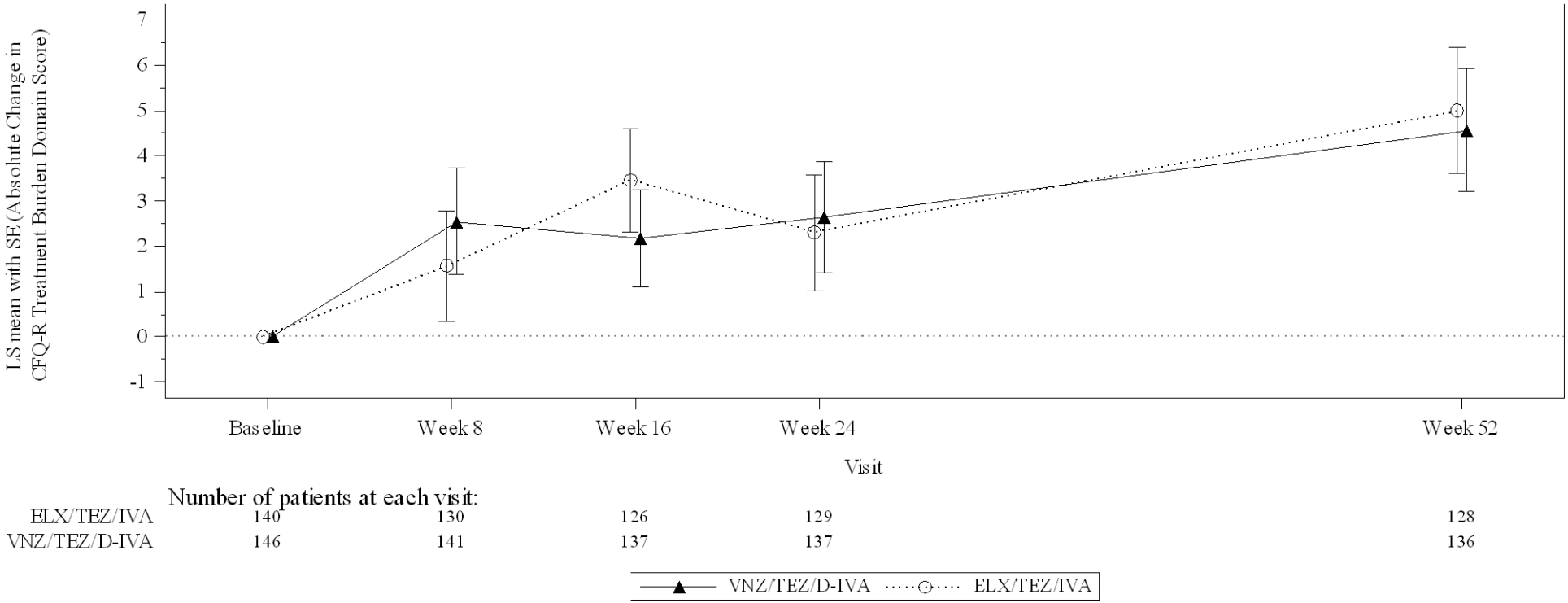
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male



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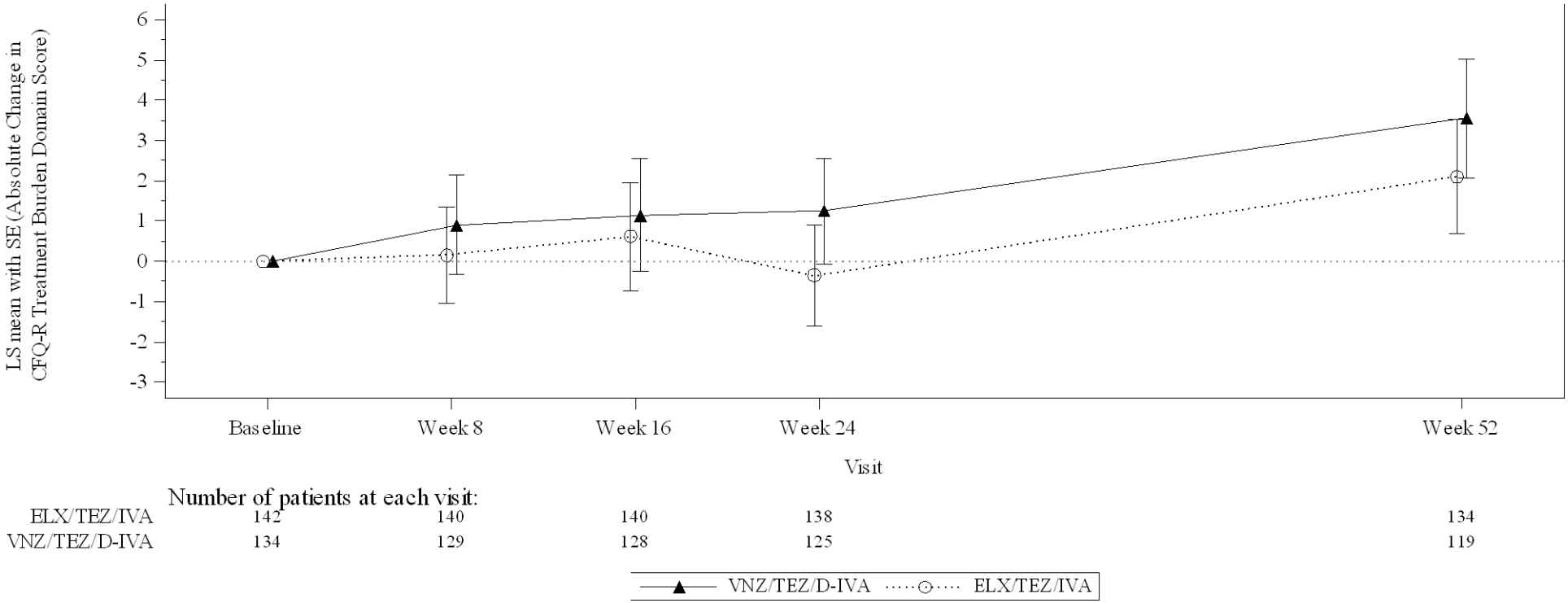
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female



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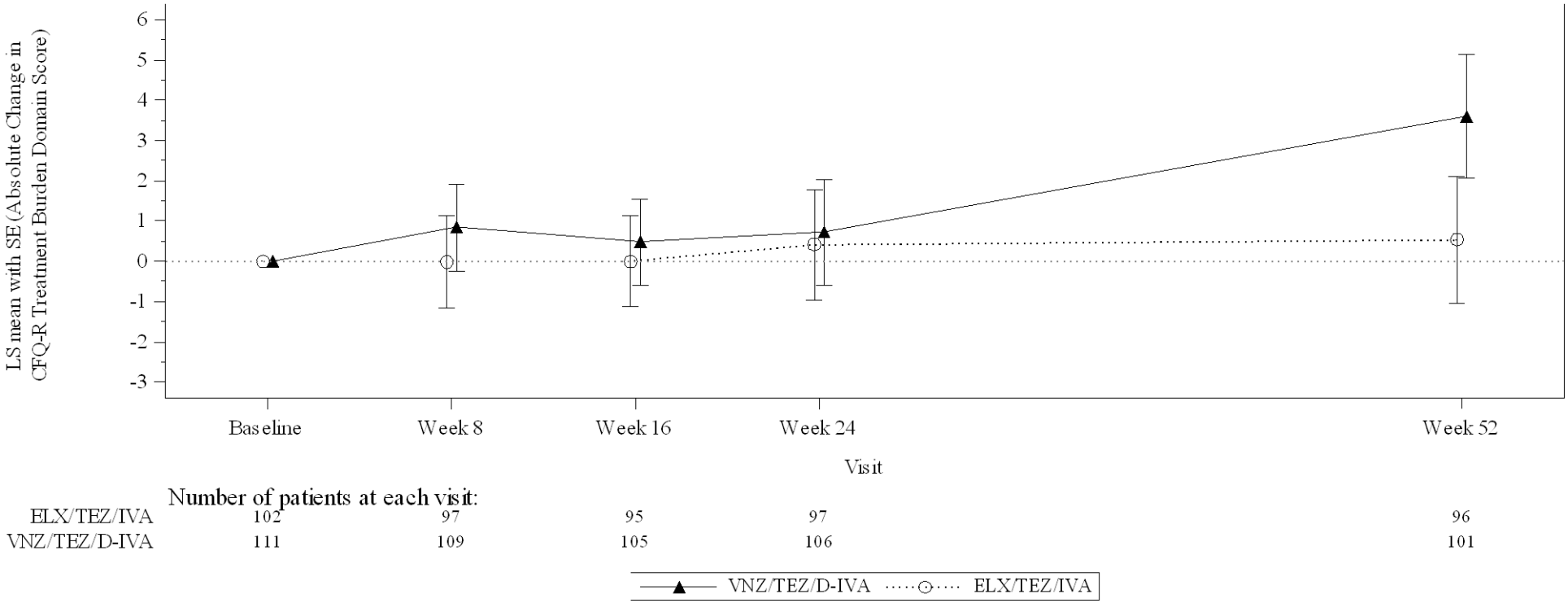
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America



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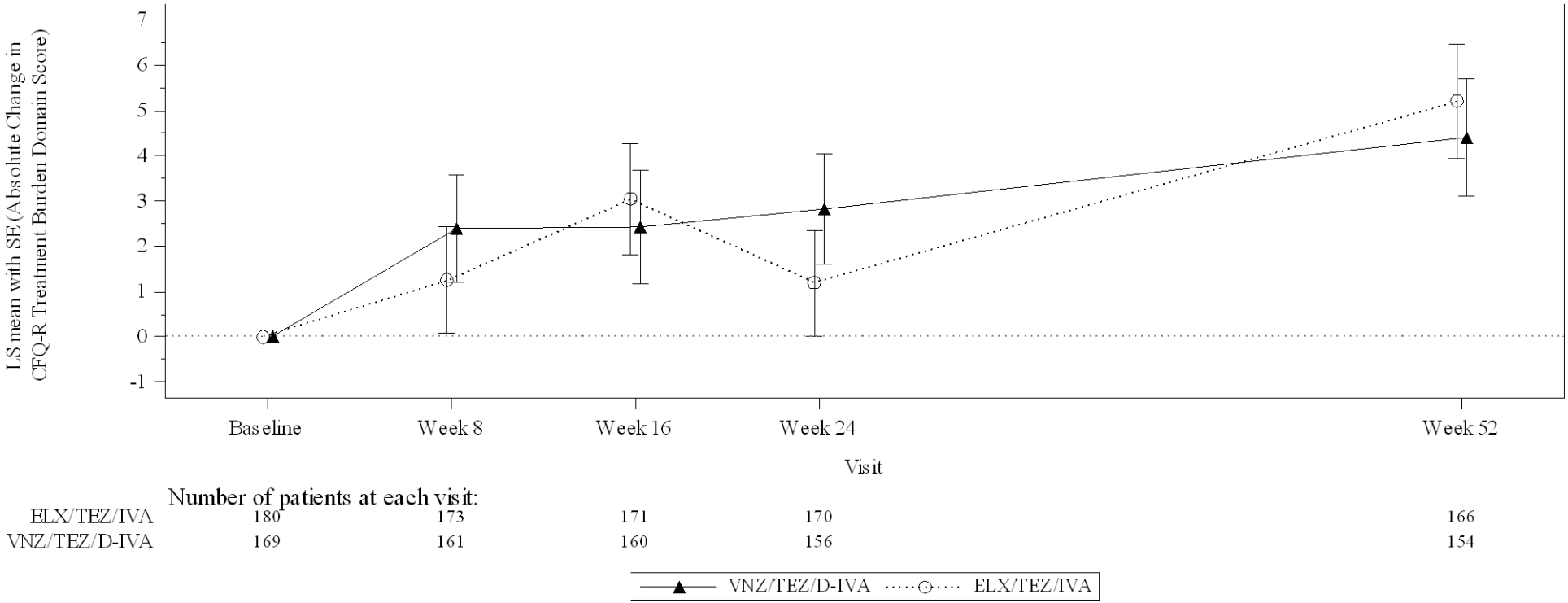
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World



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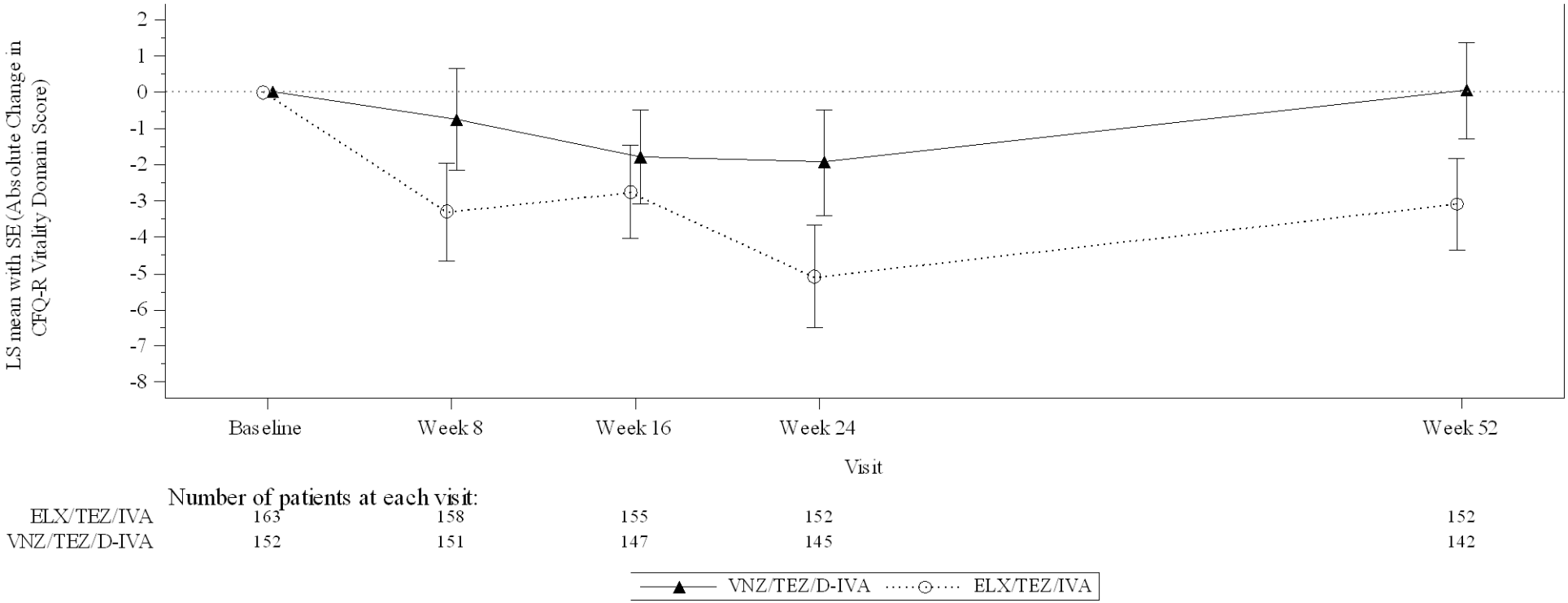
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
ppFEV$_1$ at baseline <70 %



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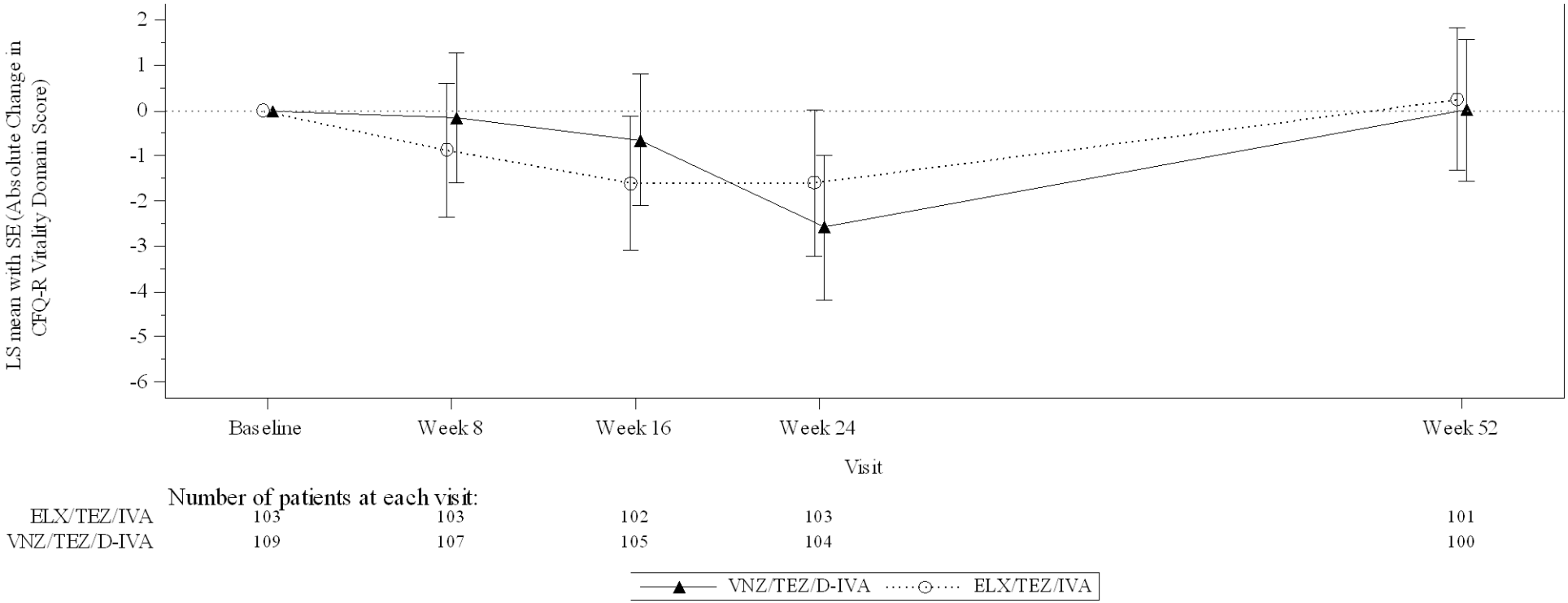
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
ppFEV$_1$ at baseline ≥70 %



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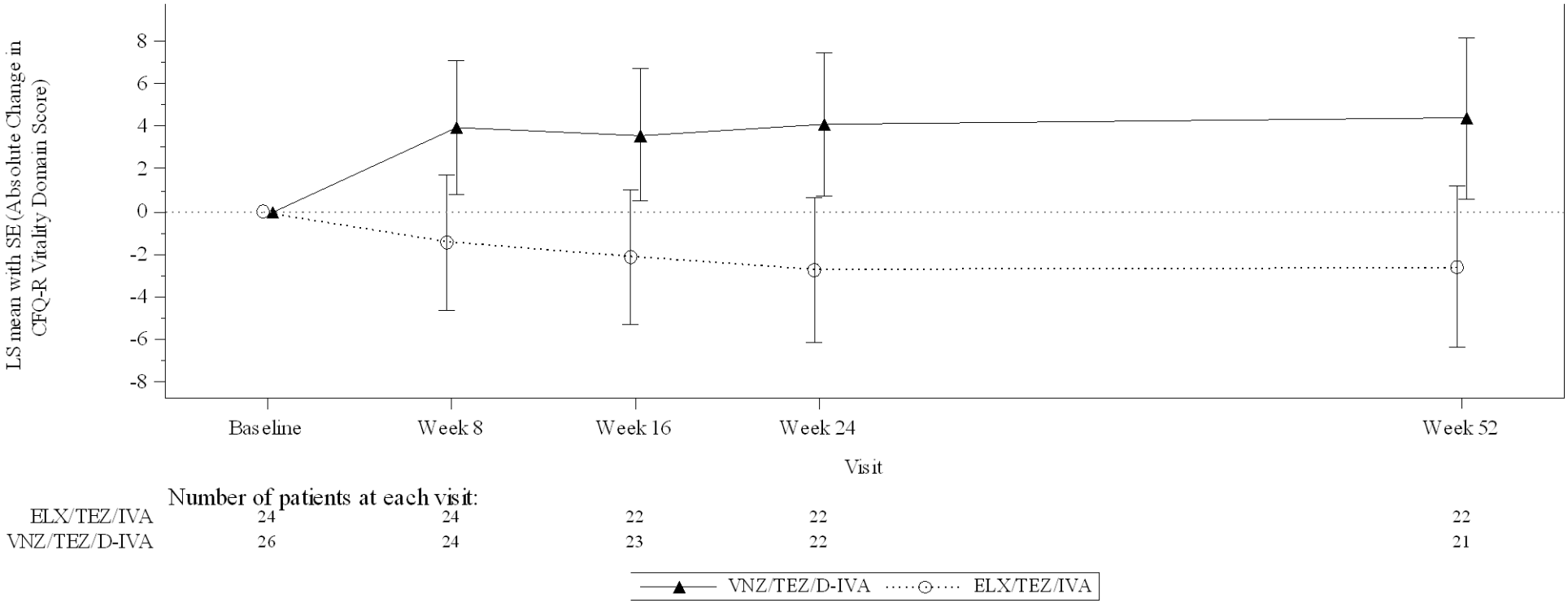
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years



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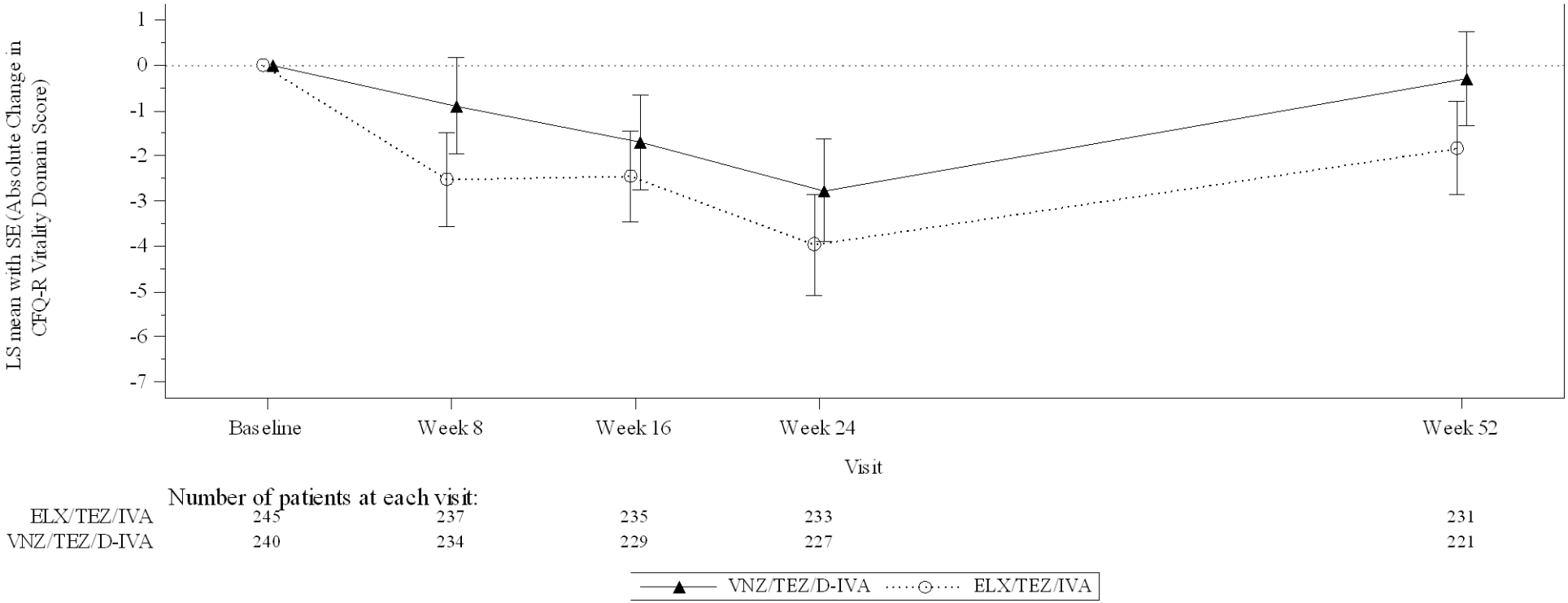
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years



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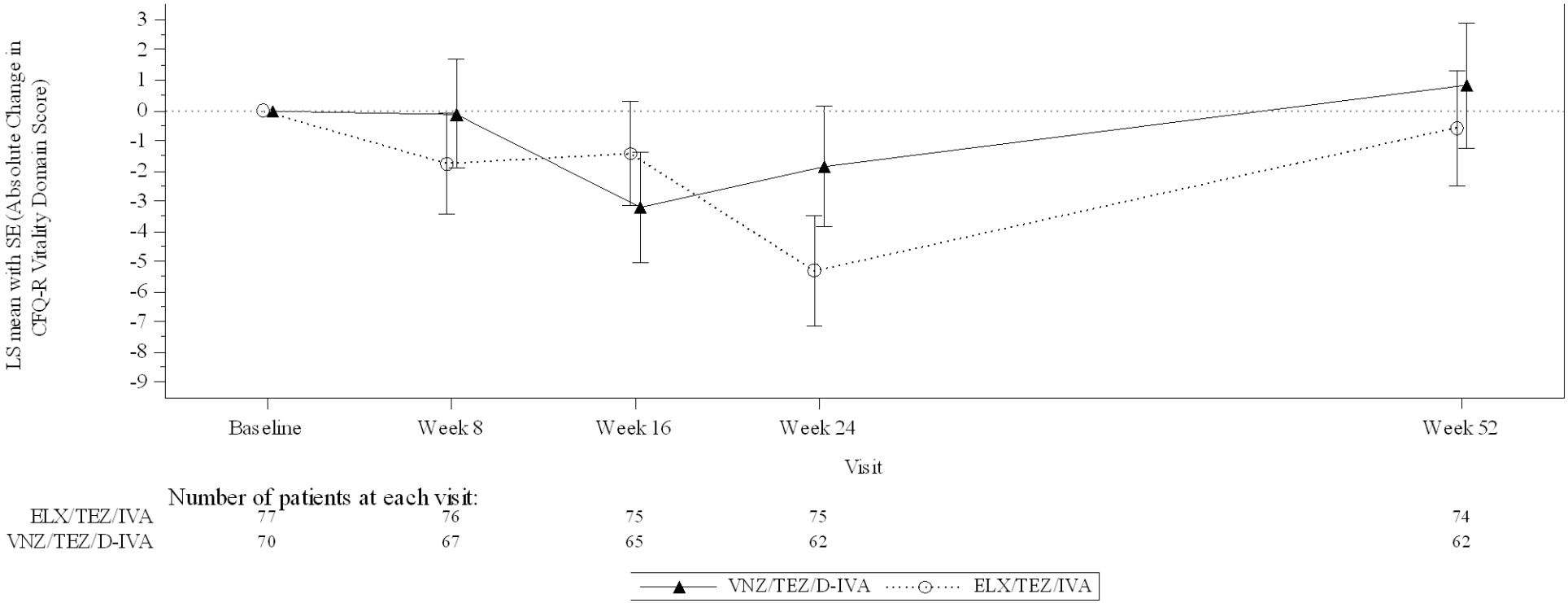
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L



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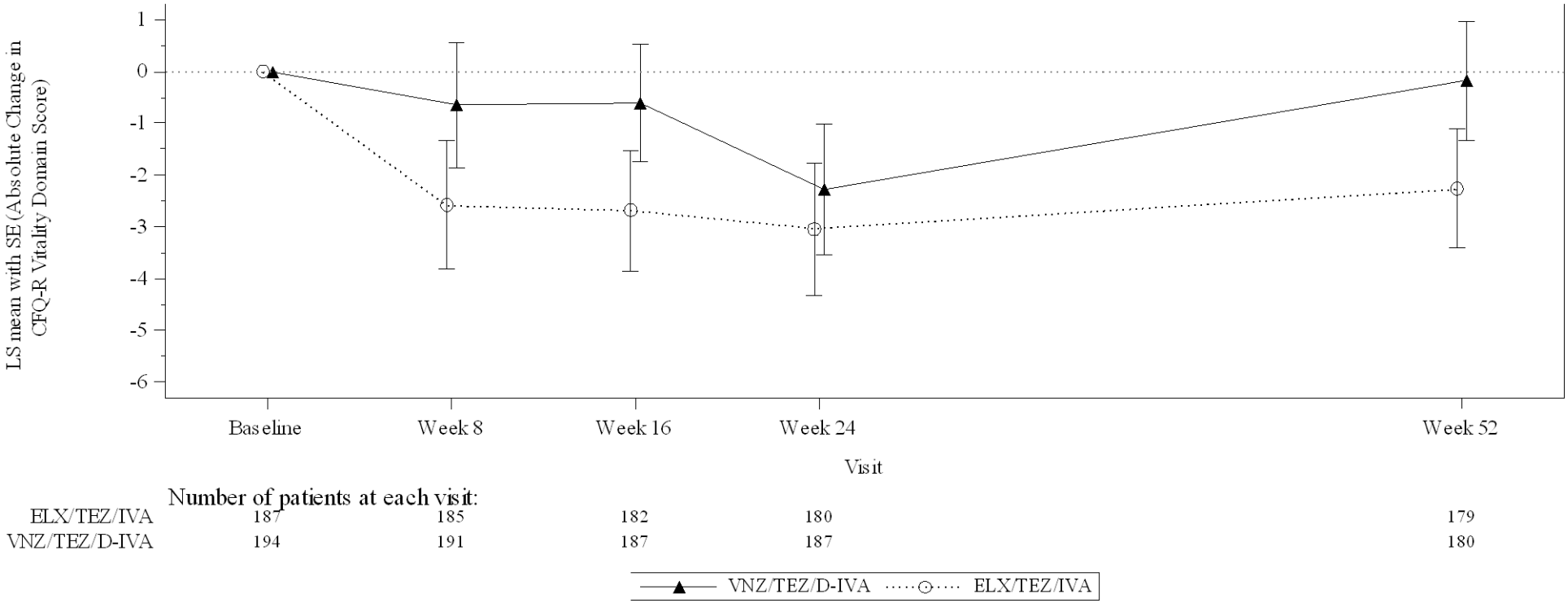
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L



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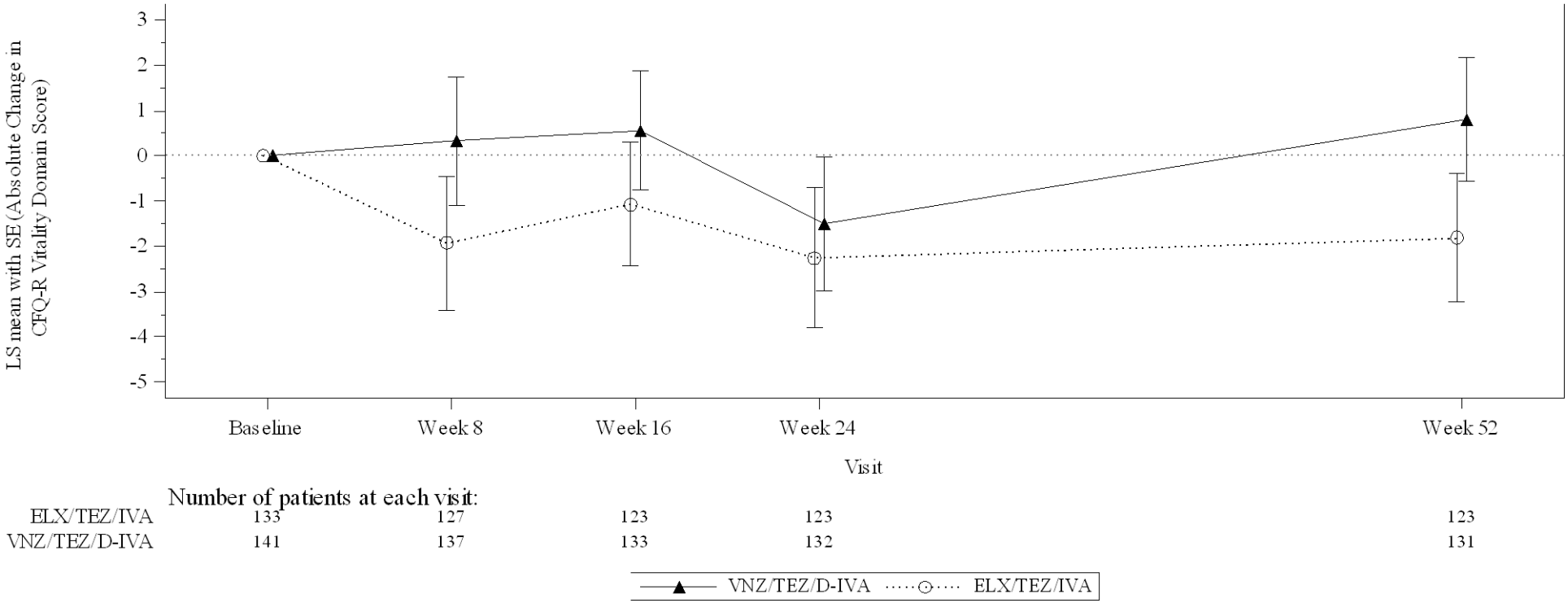
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male



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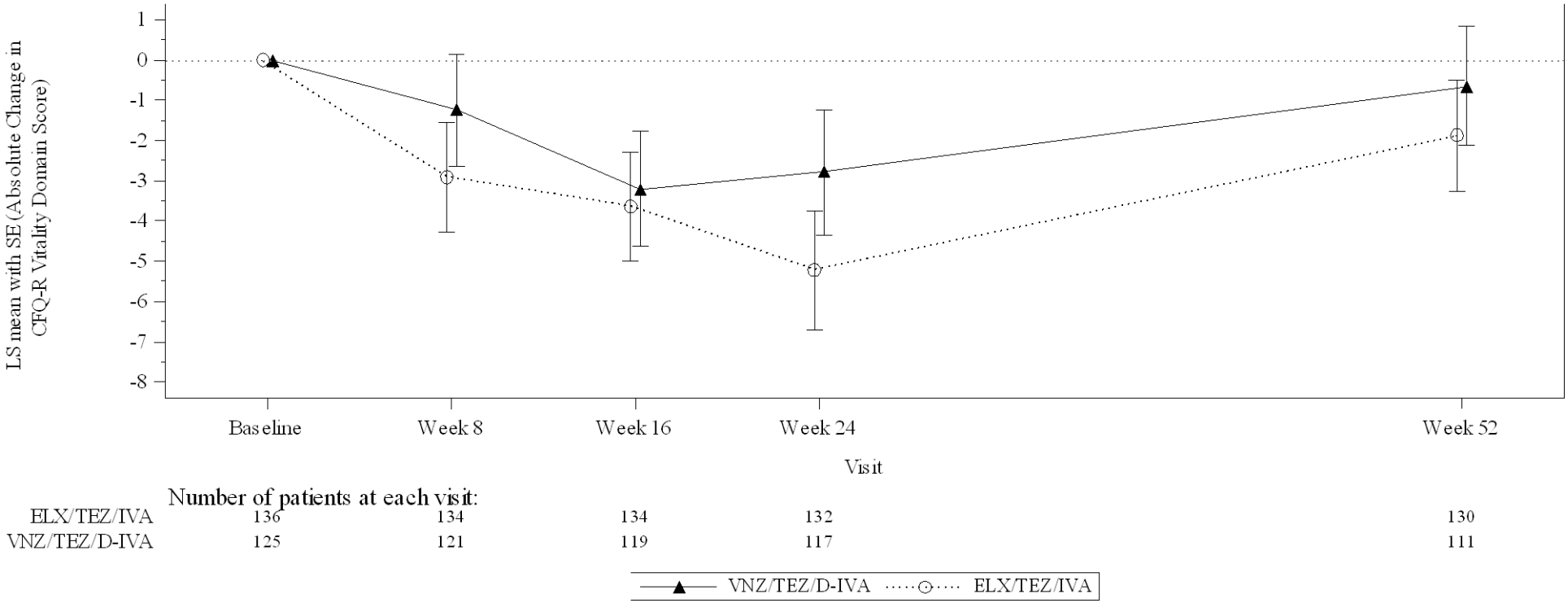
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female



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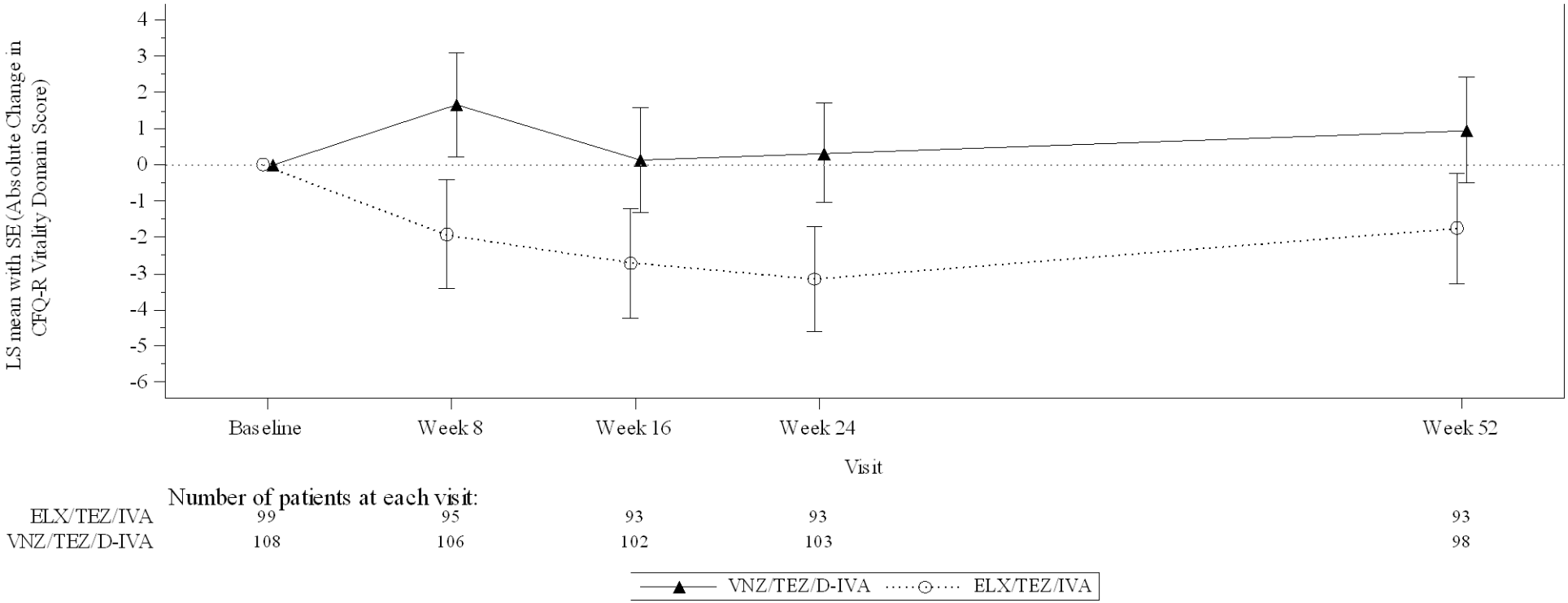
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = North America



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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World

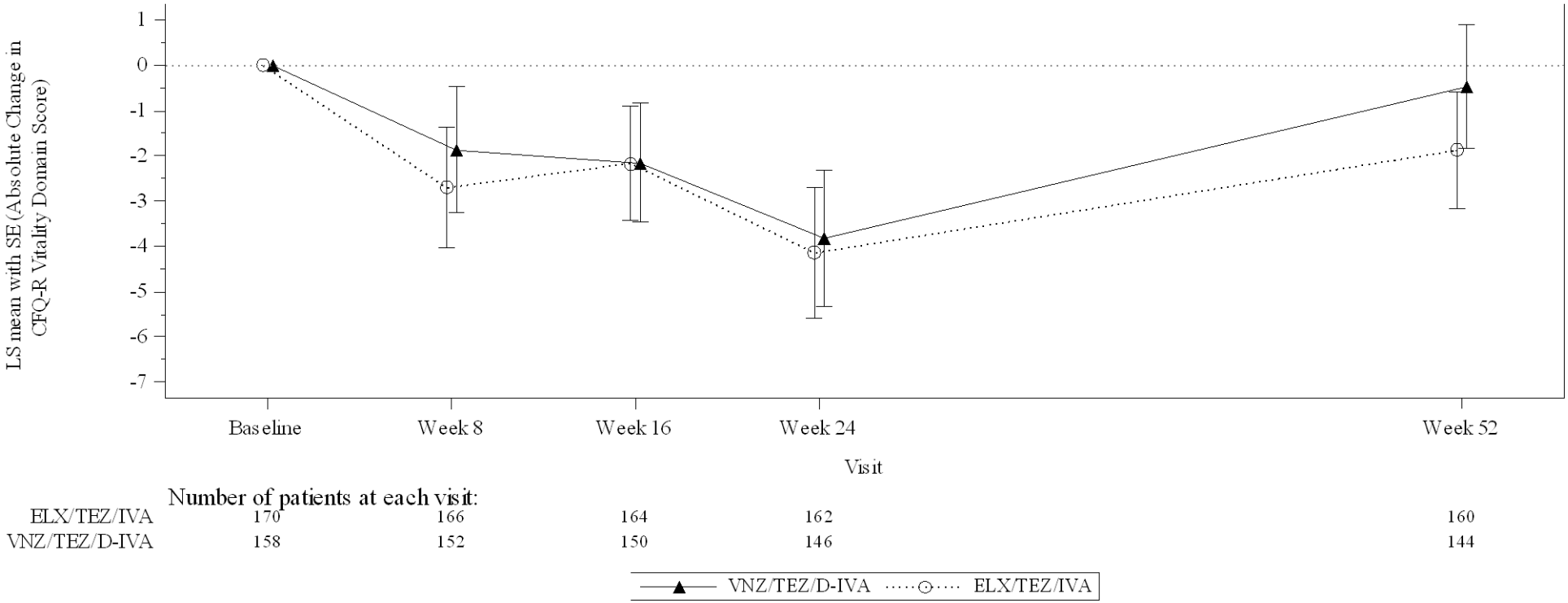

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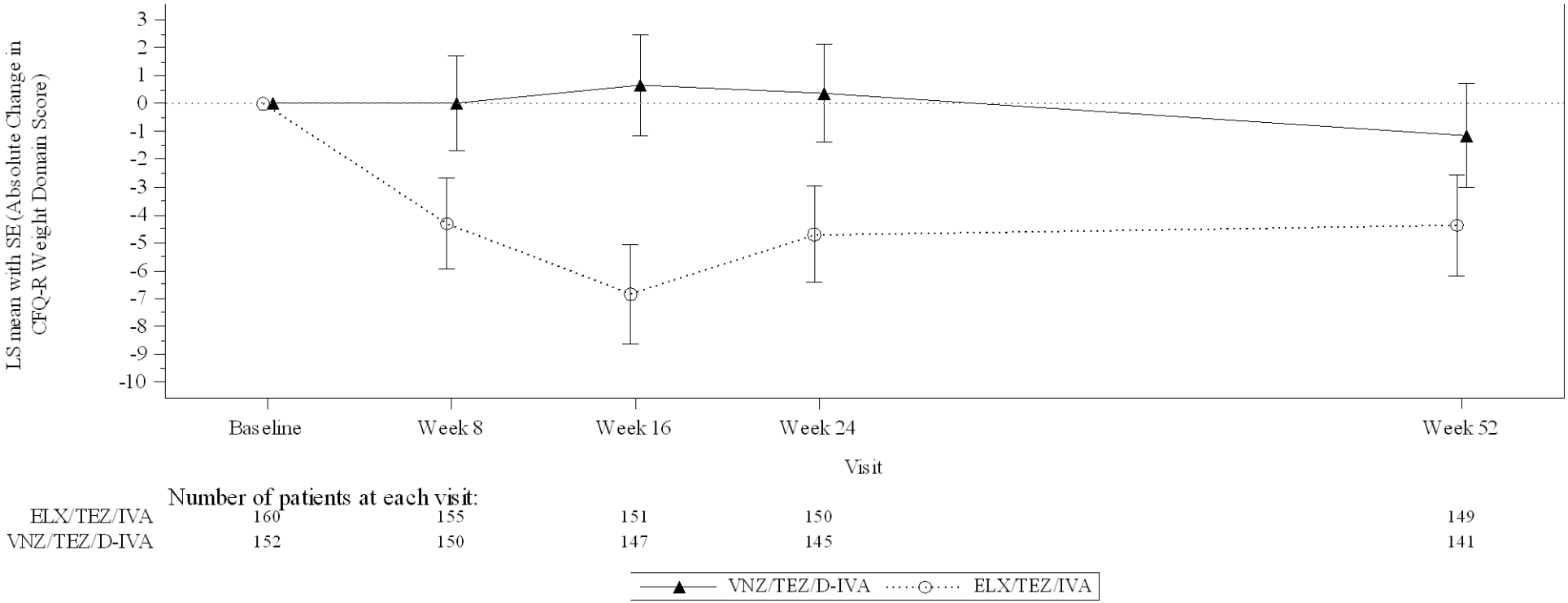
Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
ppFEV$_1$ at baseline <70 %



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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
ppFEV$_1$ at baseline ≥70 %

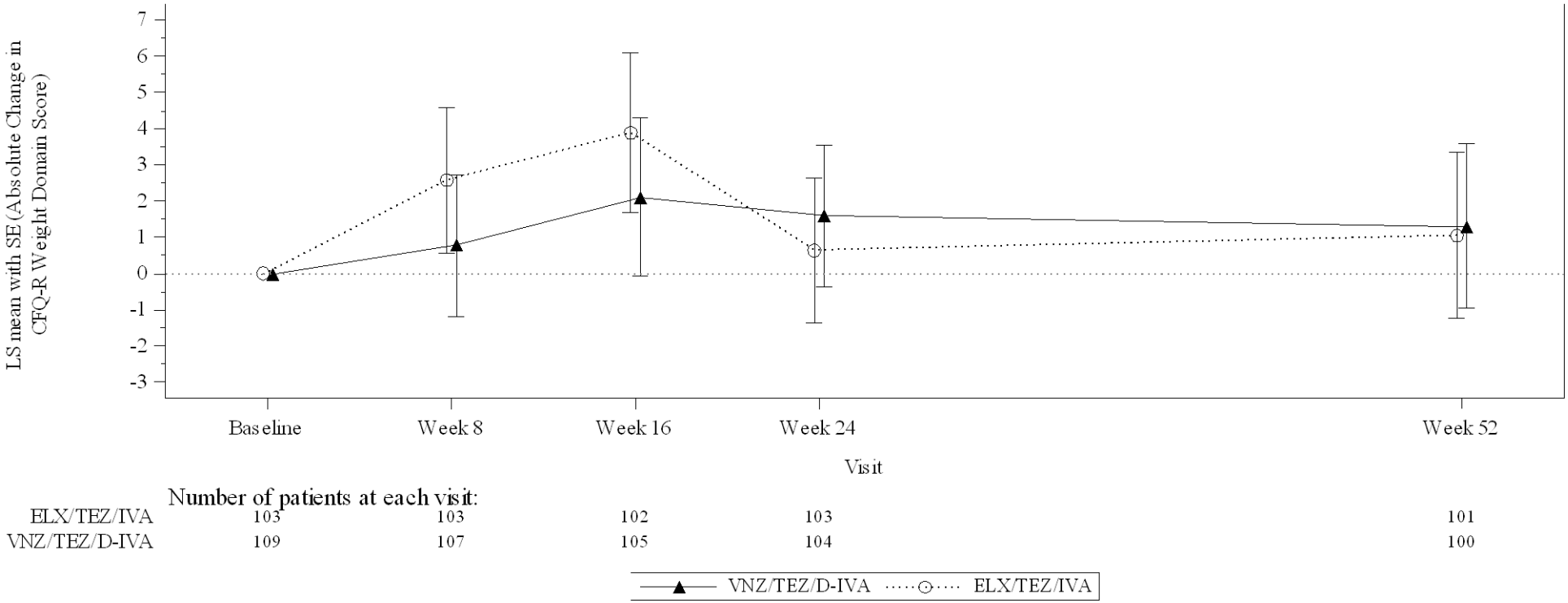

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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years

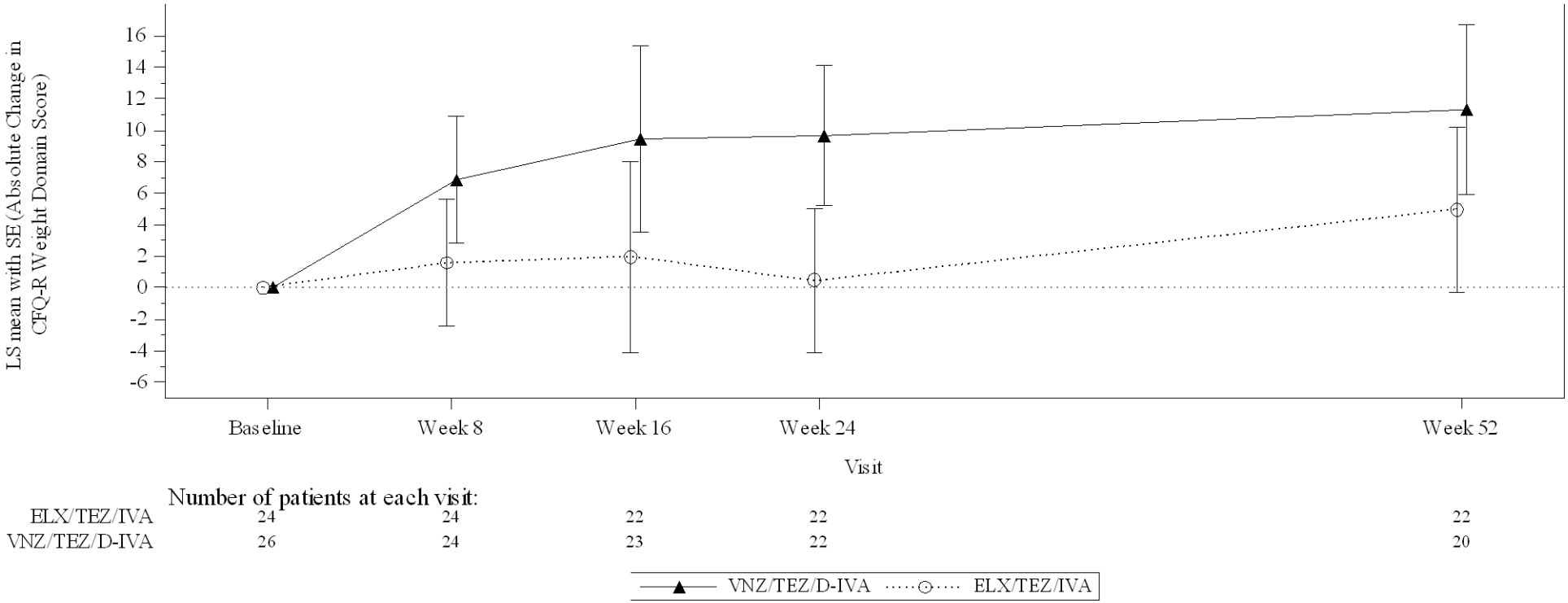

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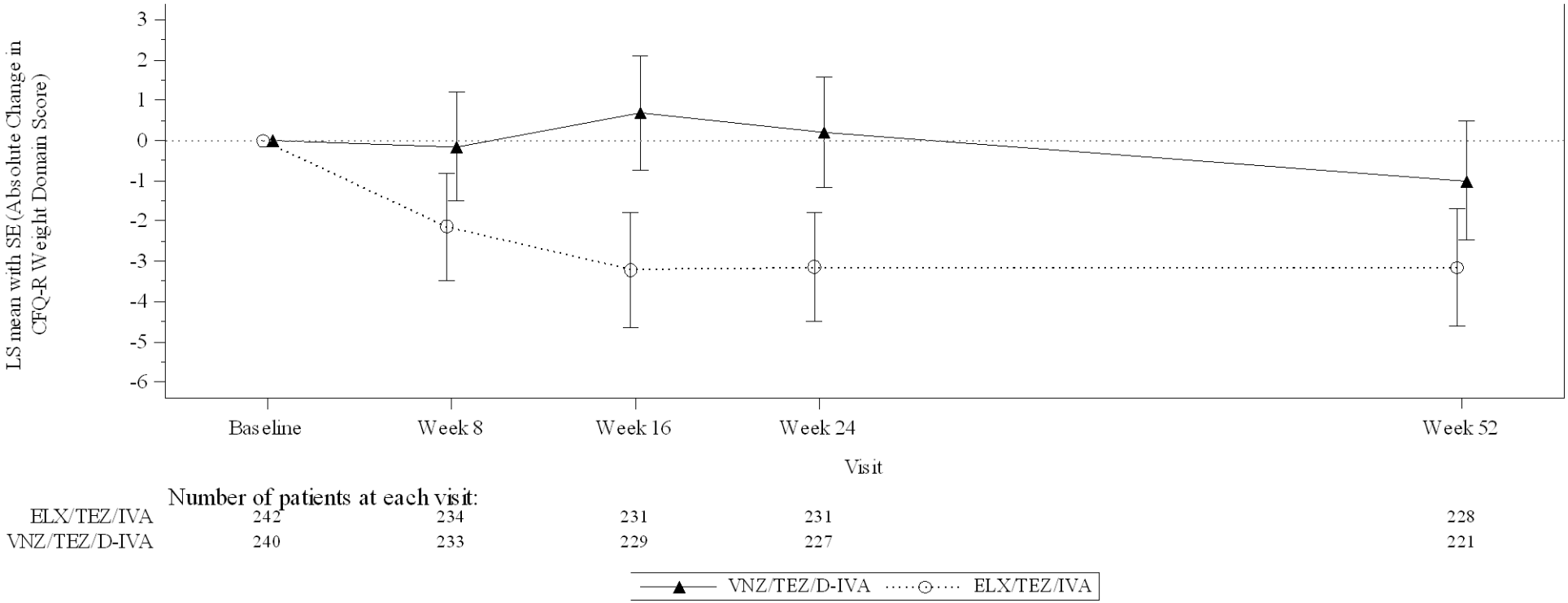
Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years



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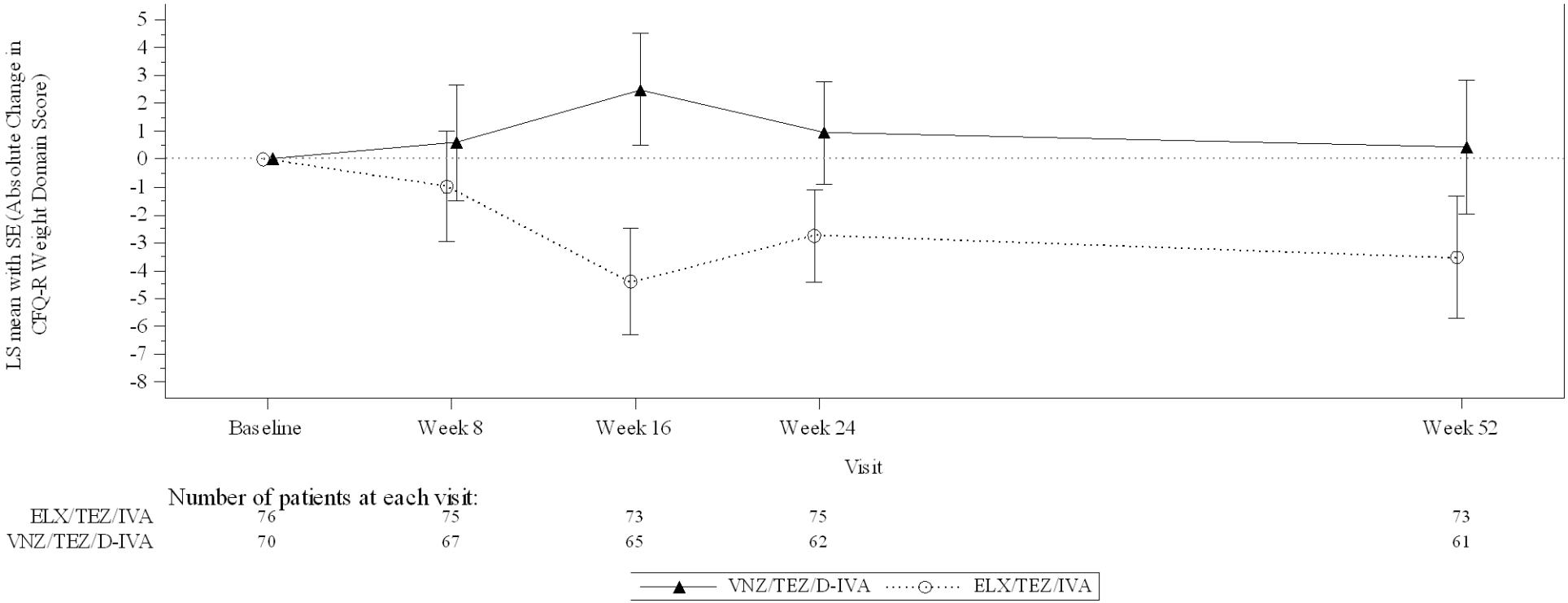
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L



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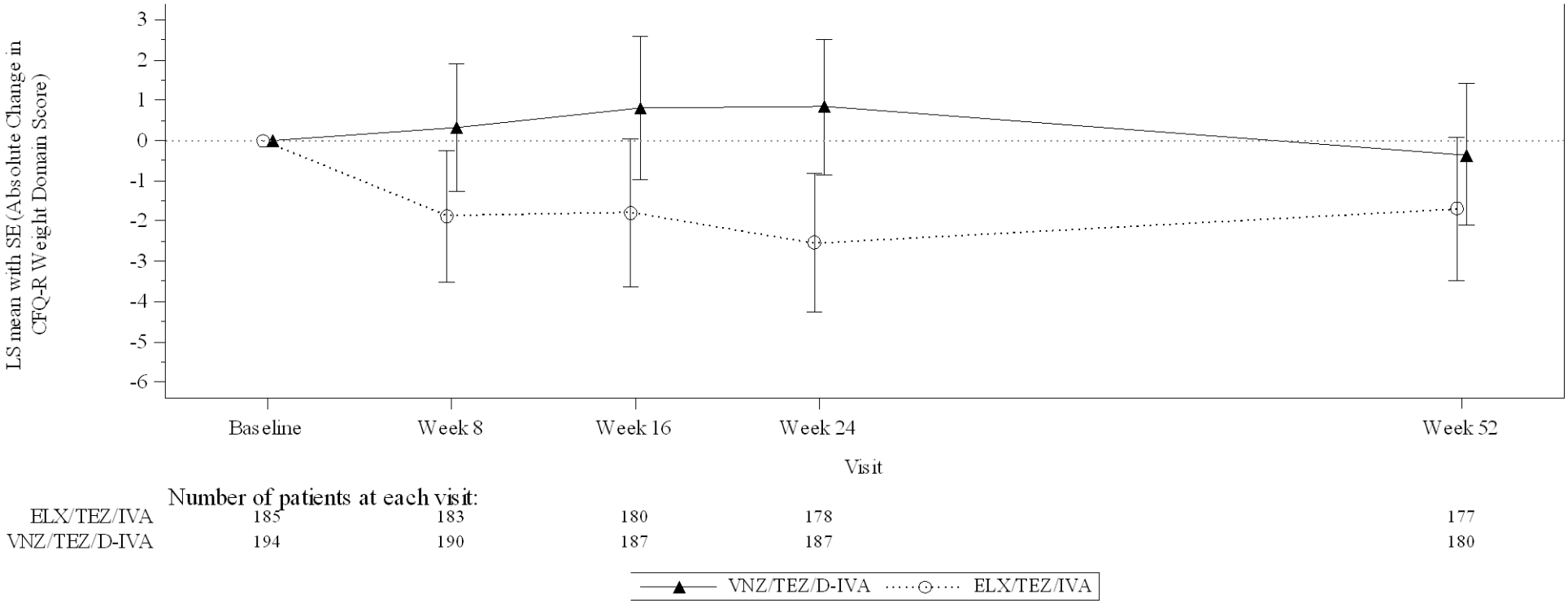
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L



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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Male

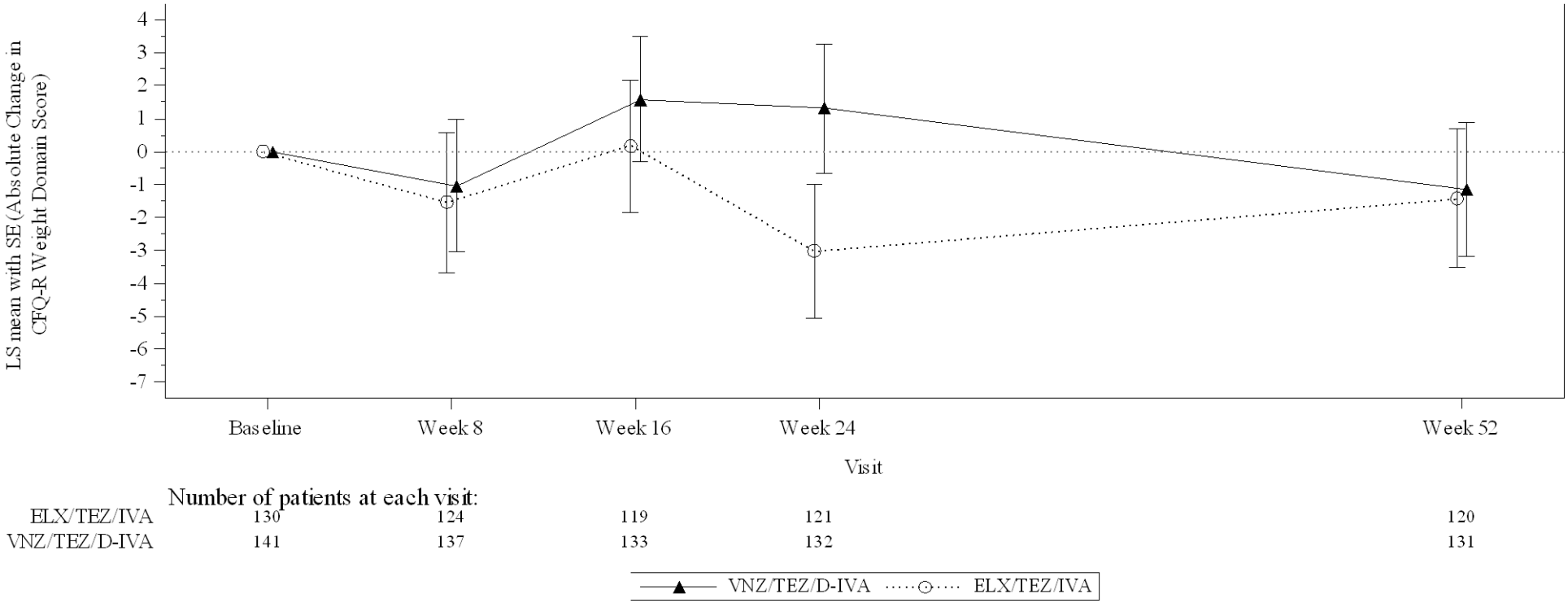

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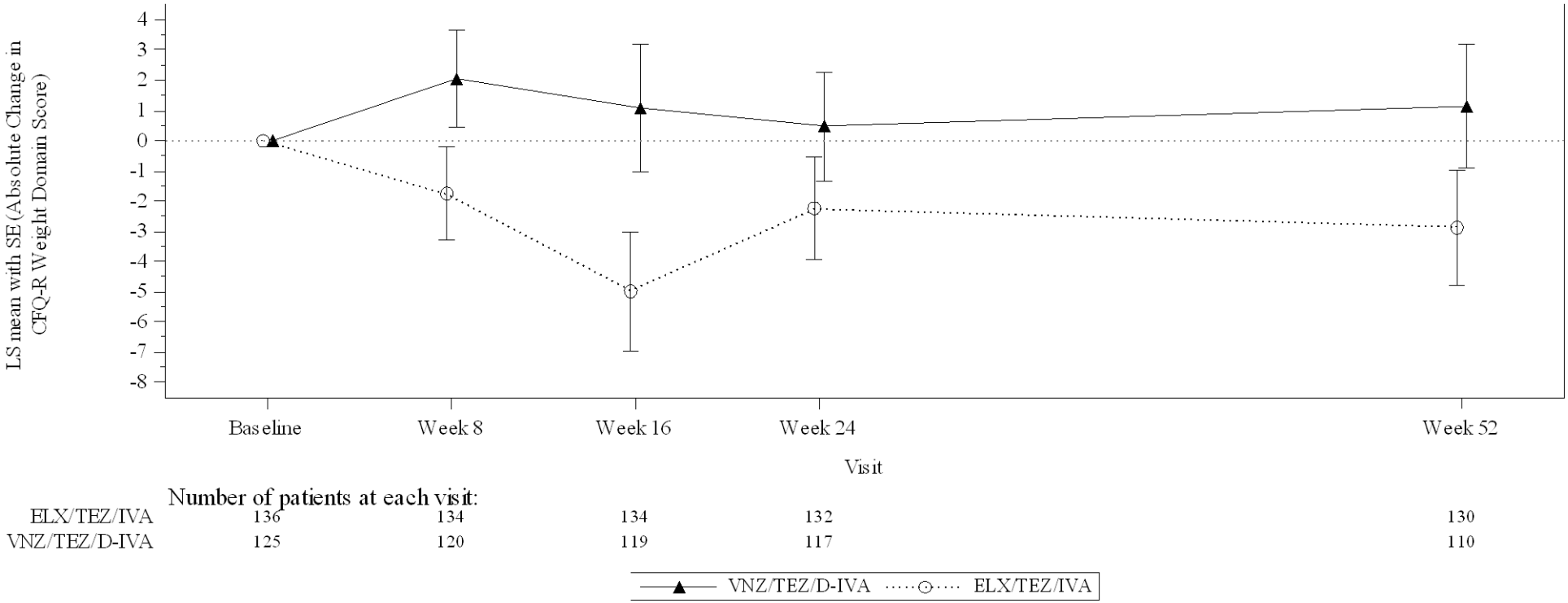
Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Female



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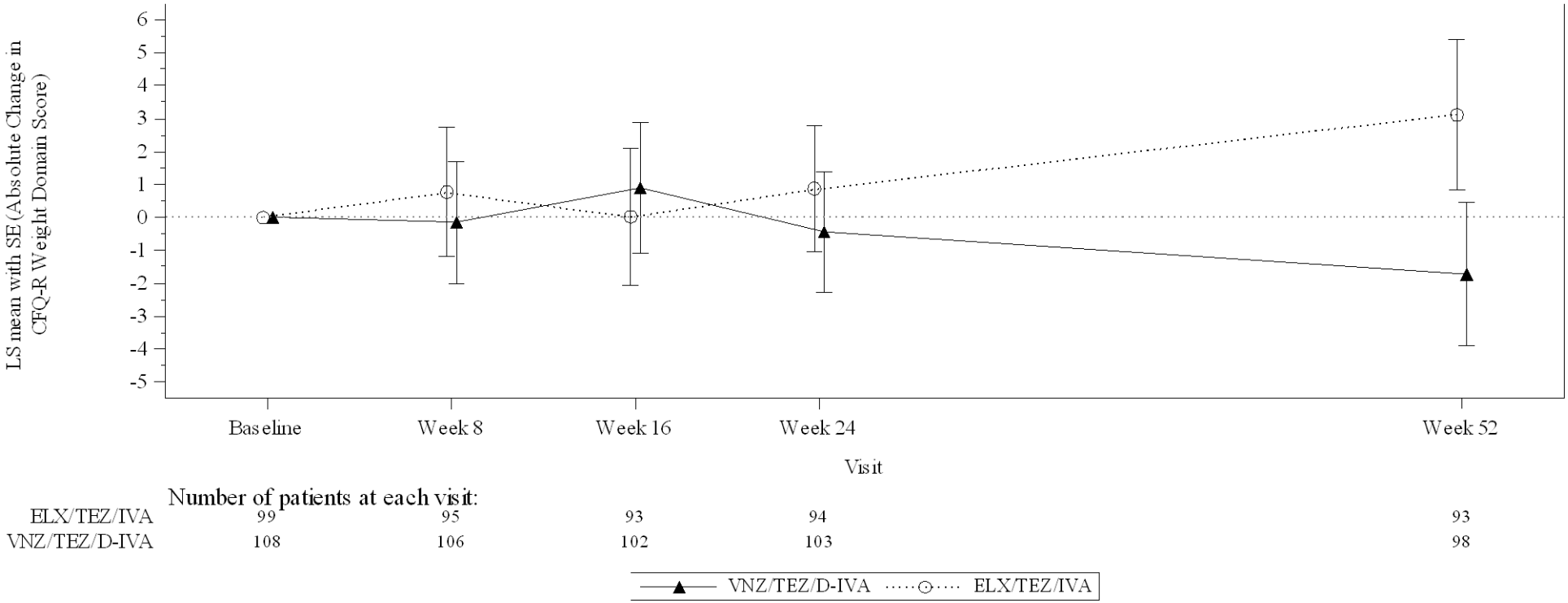
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = North America



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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World

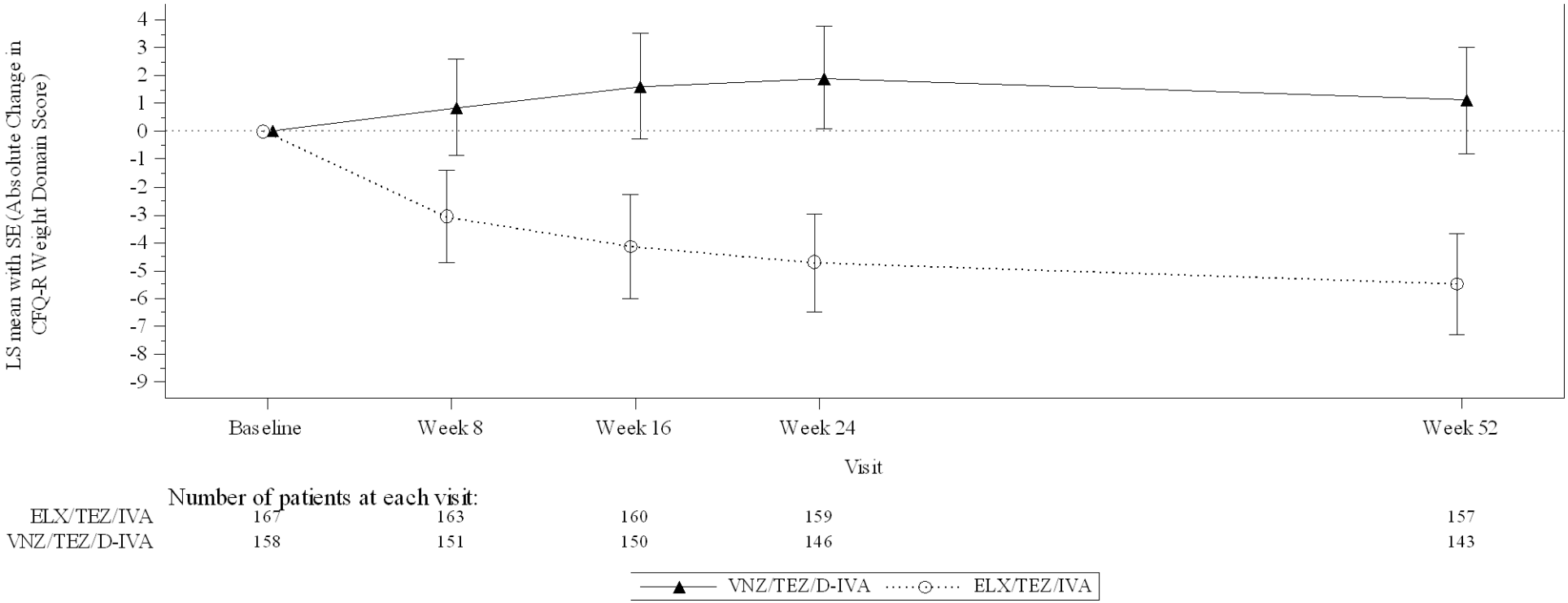

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)
Sex = Female

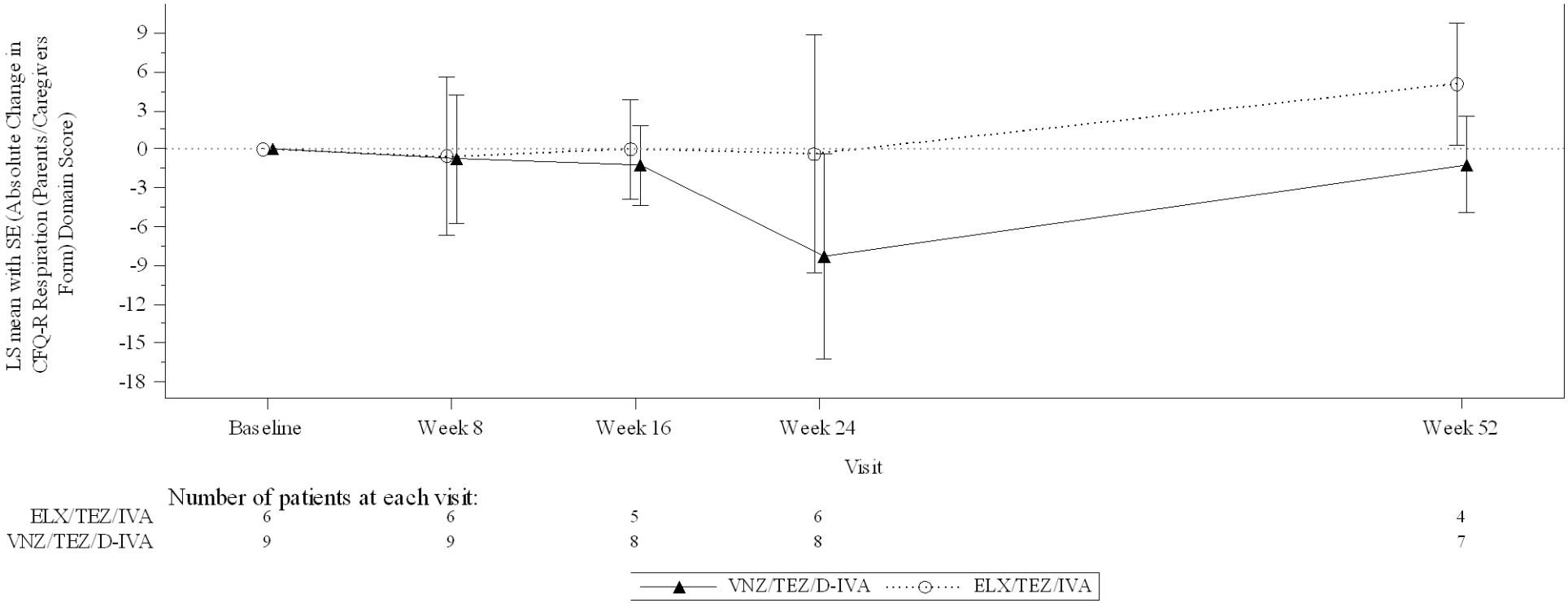

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)
ppFEV$_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)
Sex = Male

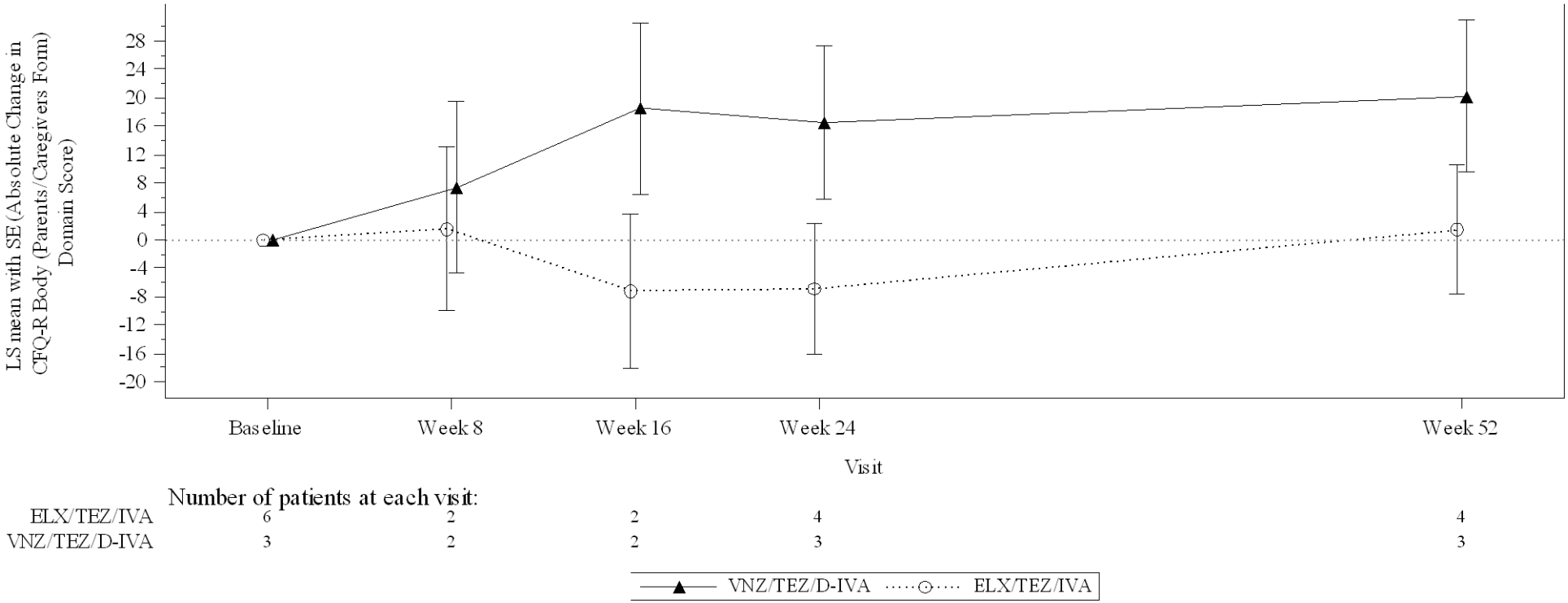

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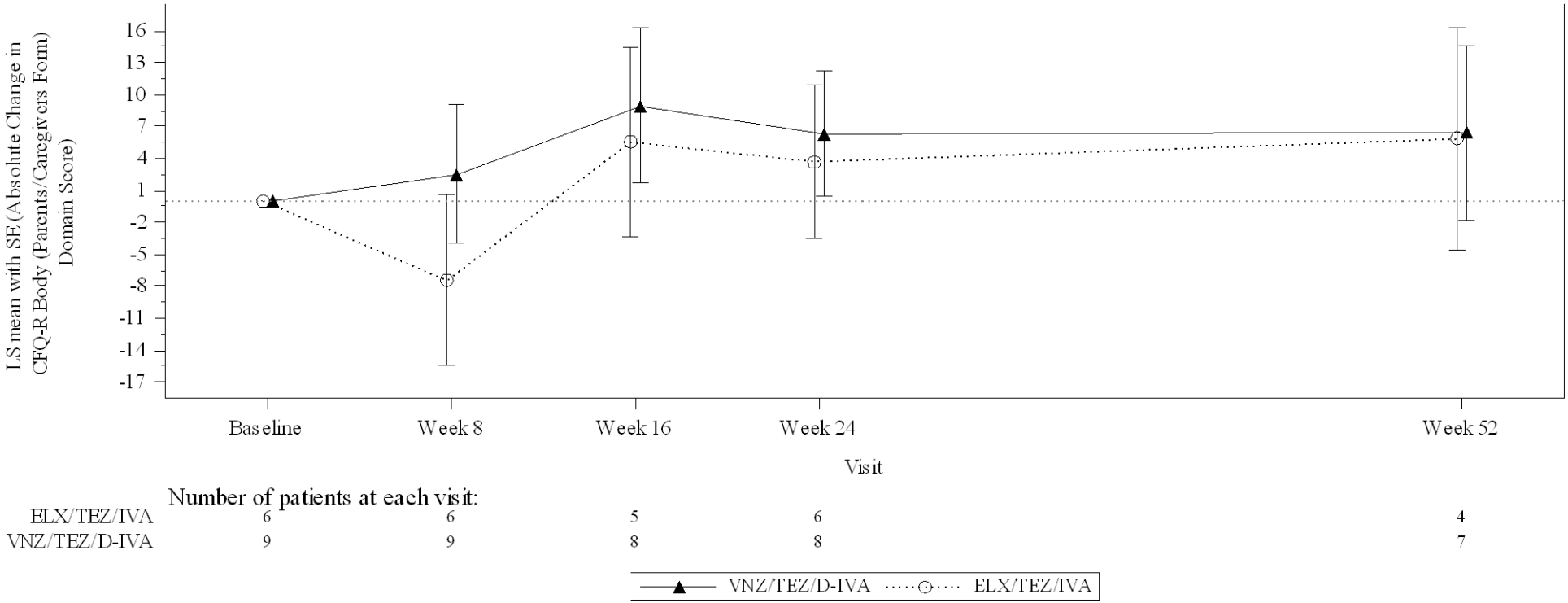
Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)
Sex = Female



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- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)
ppFEV$_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)
Sex = Male

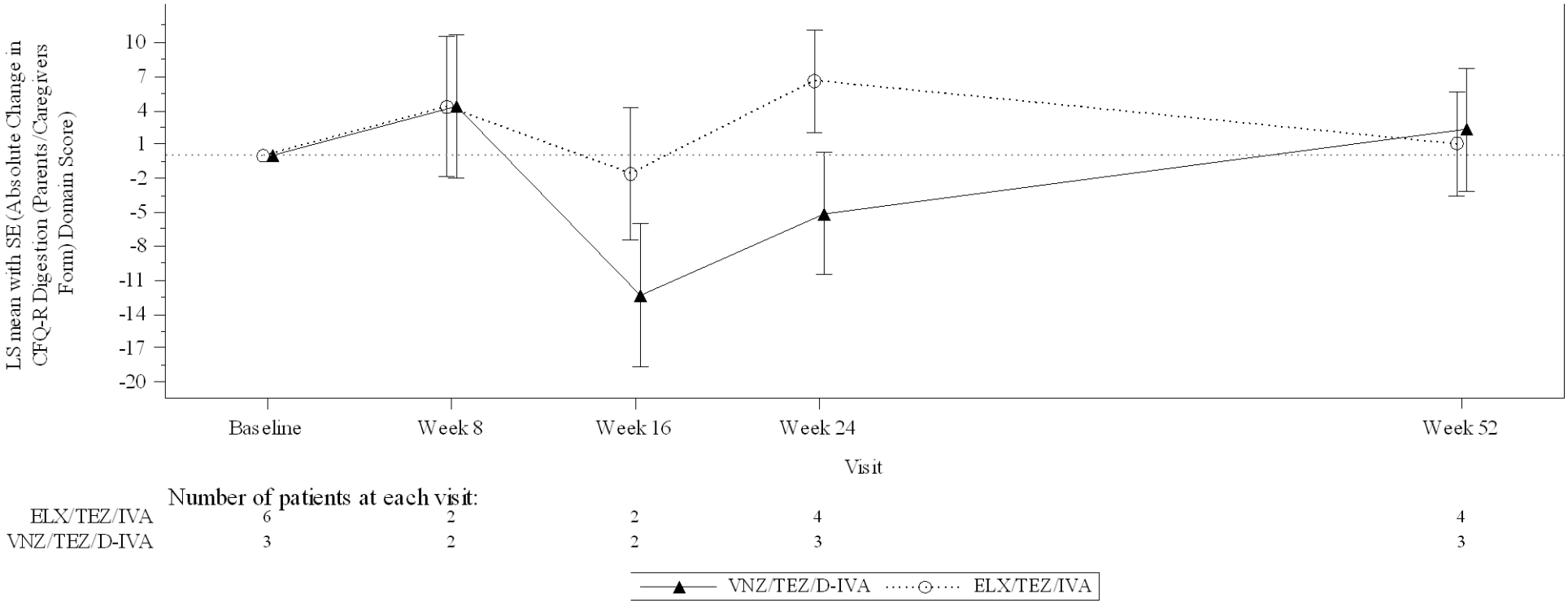

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)
Sex = Female

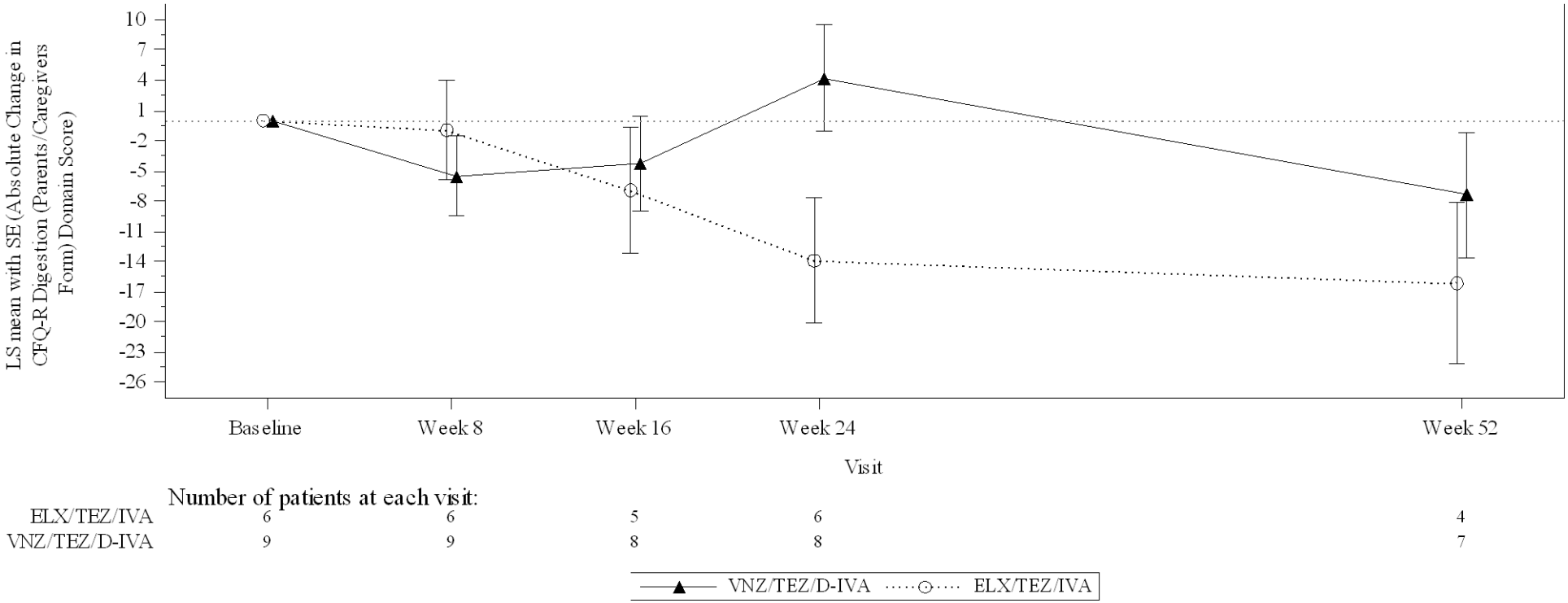

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)
ppFEV$_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)
Sex = Male

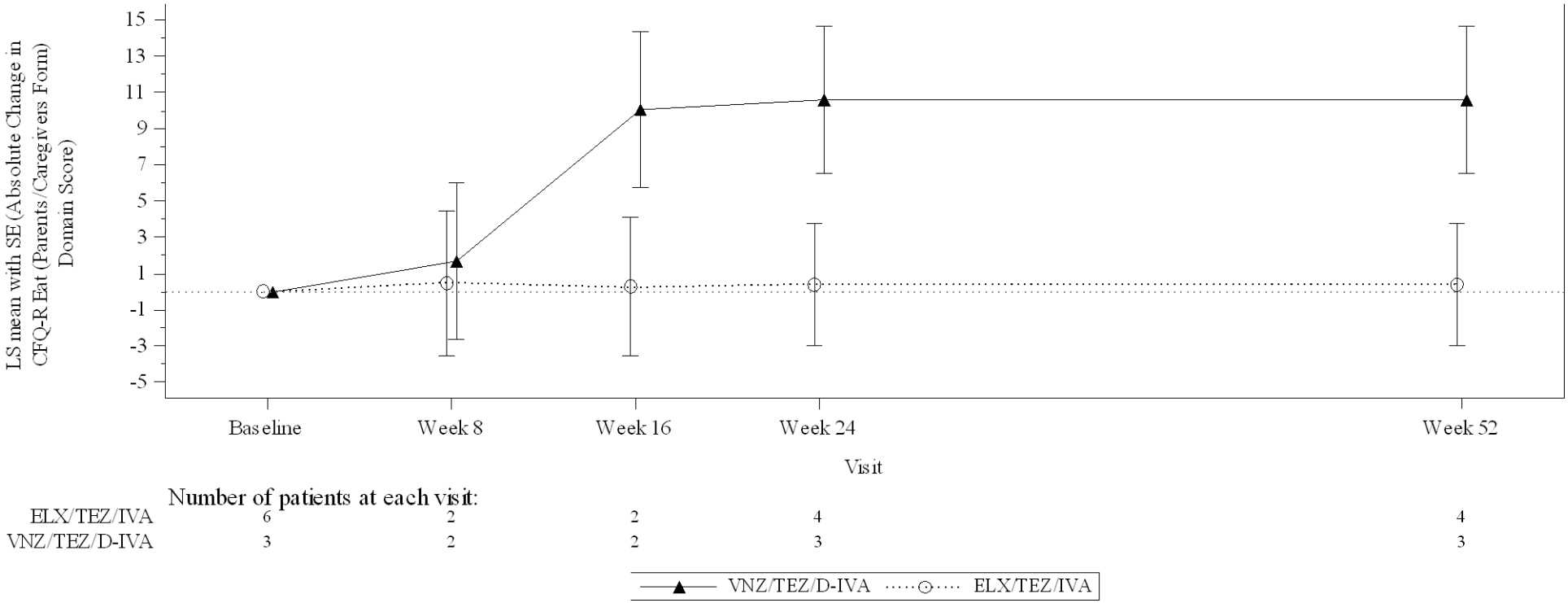

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)
Sex = Female

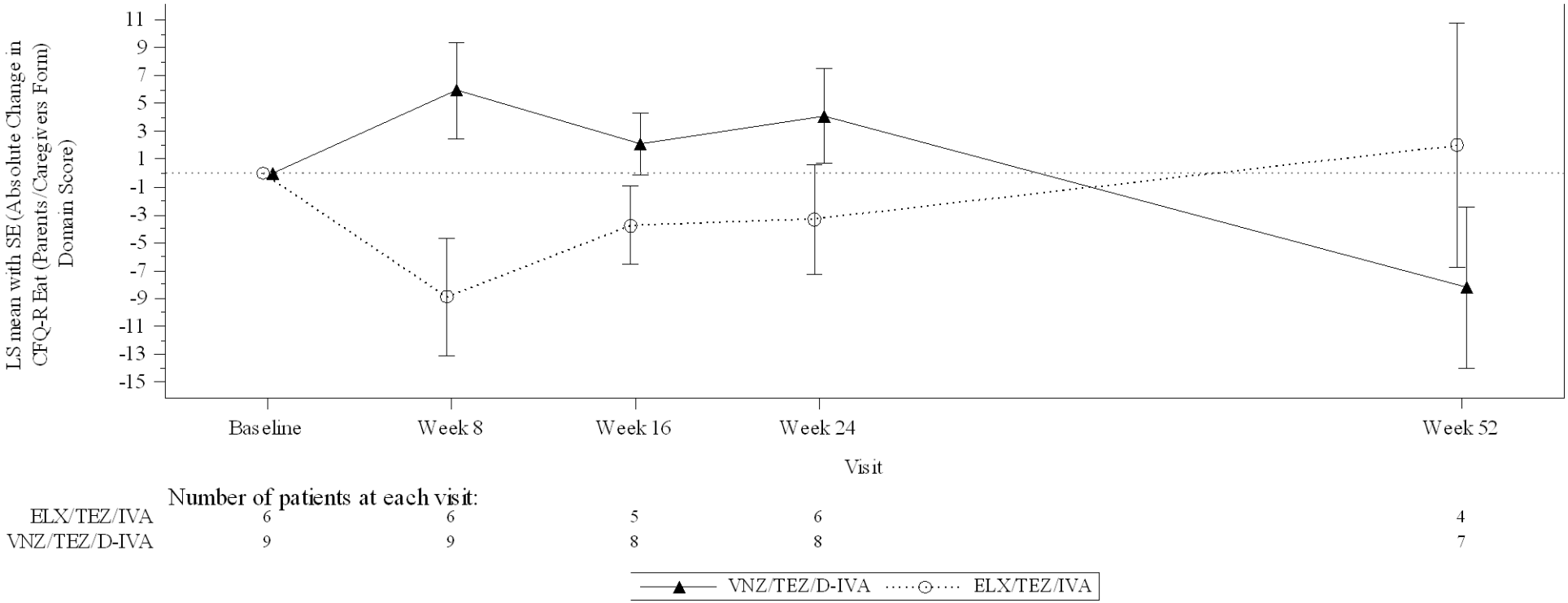

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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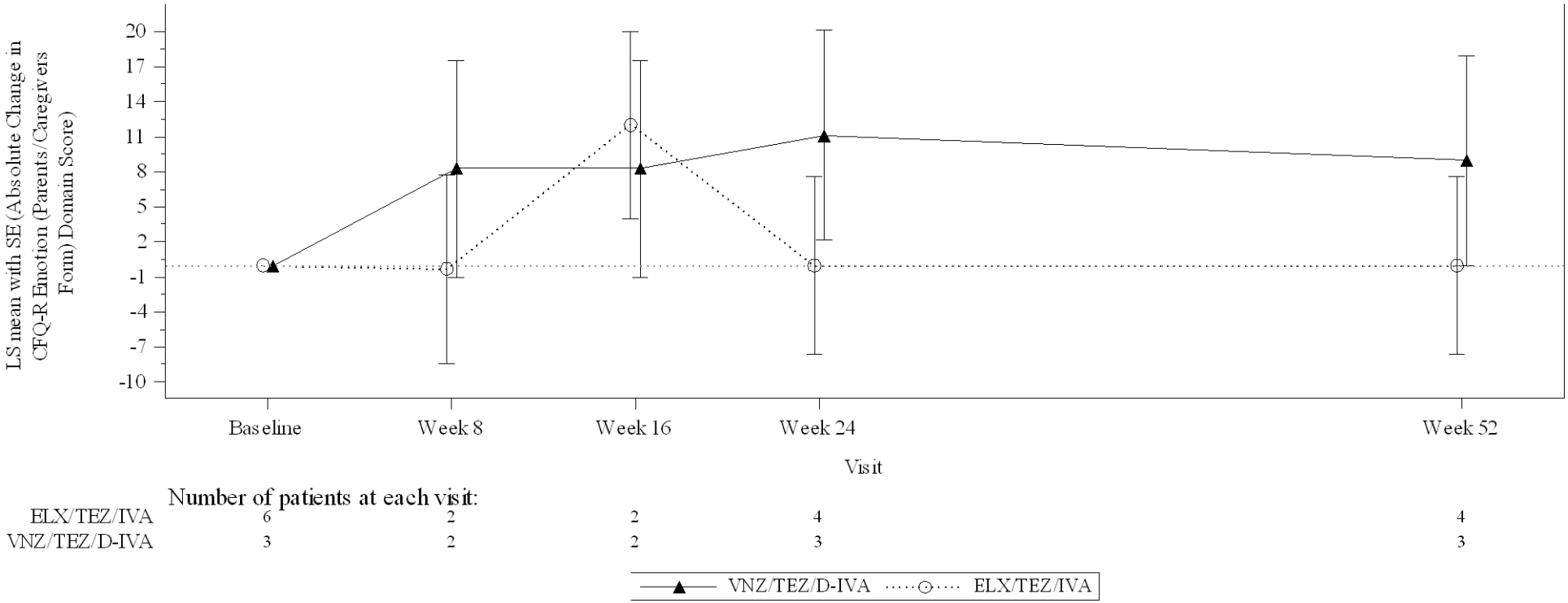
Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)
Sex = Male



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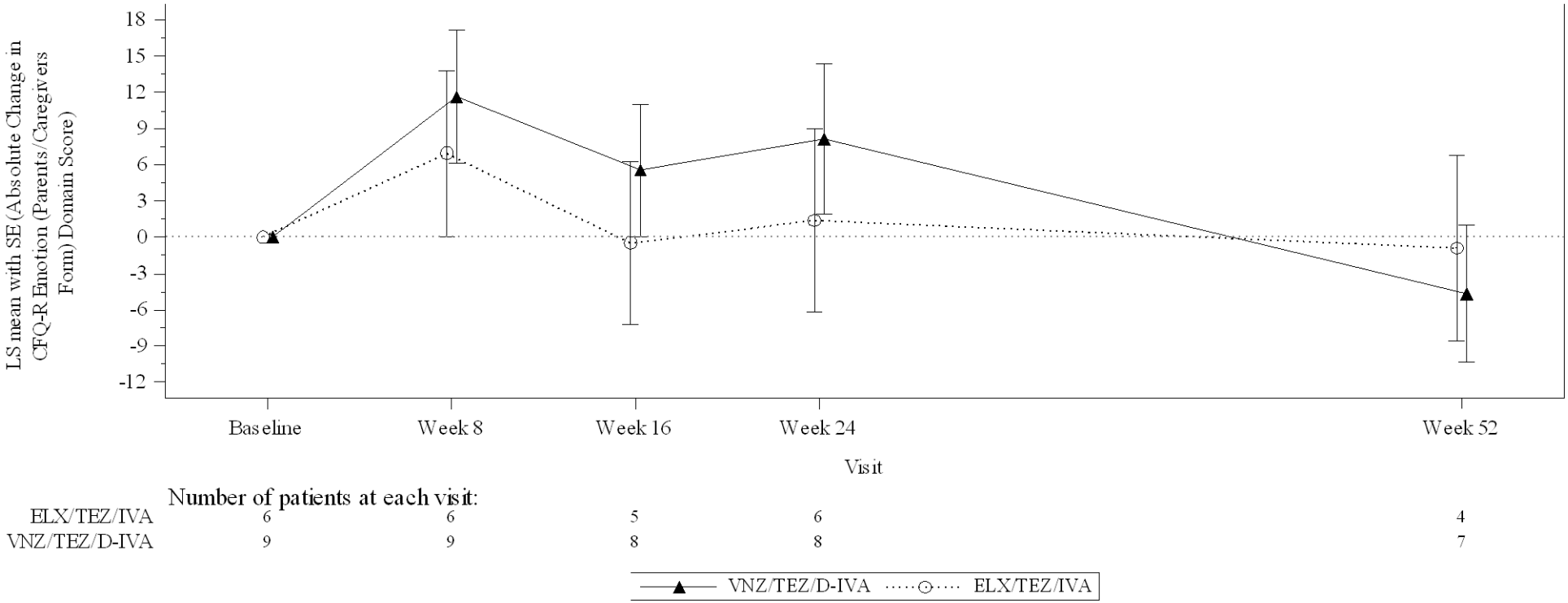
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)
Sex = Female



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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

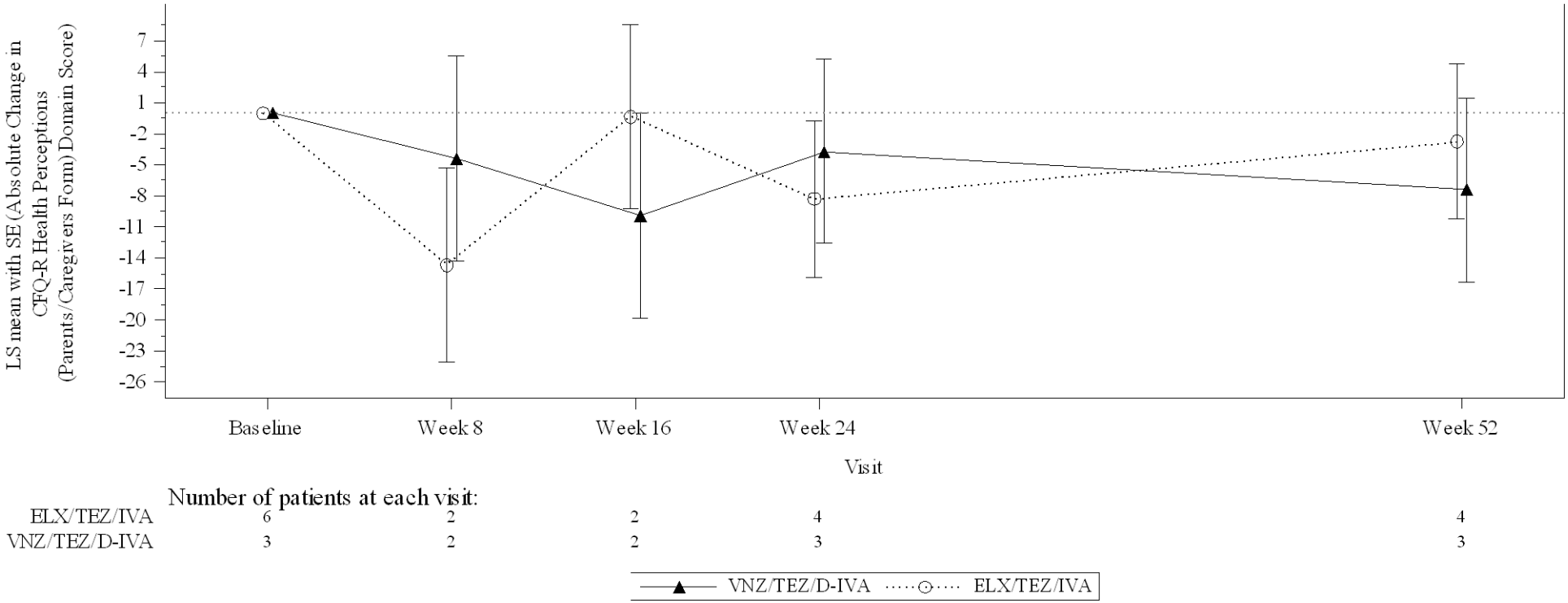

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

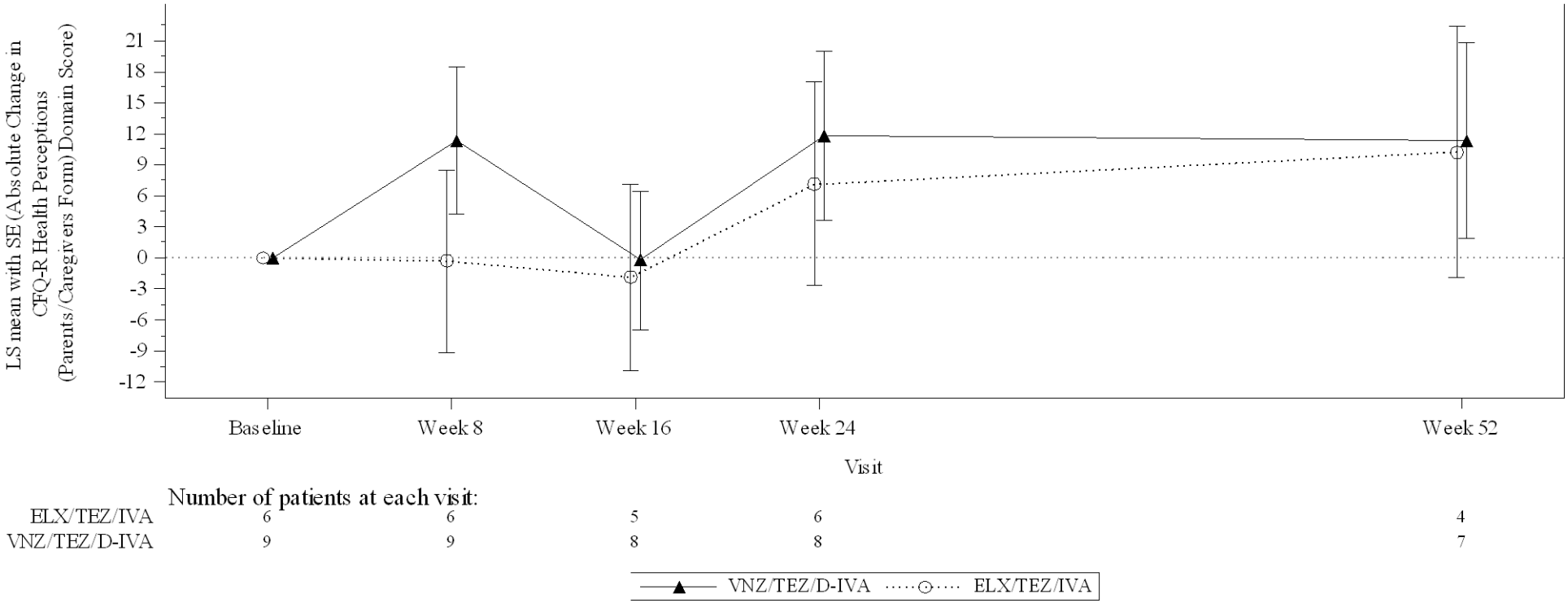

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)
ppFEV$_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)
Sex = Male

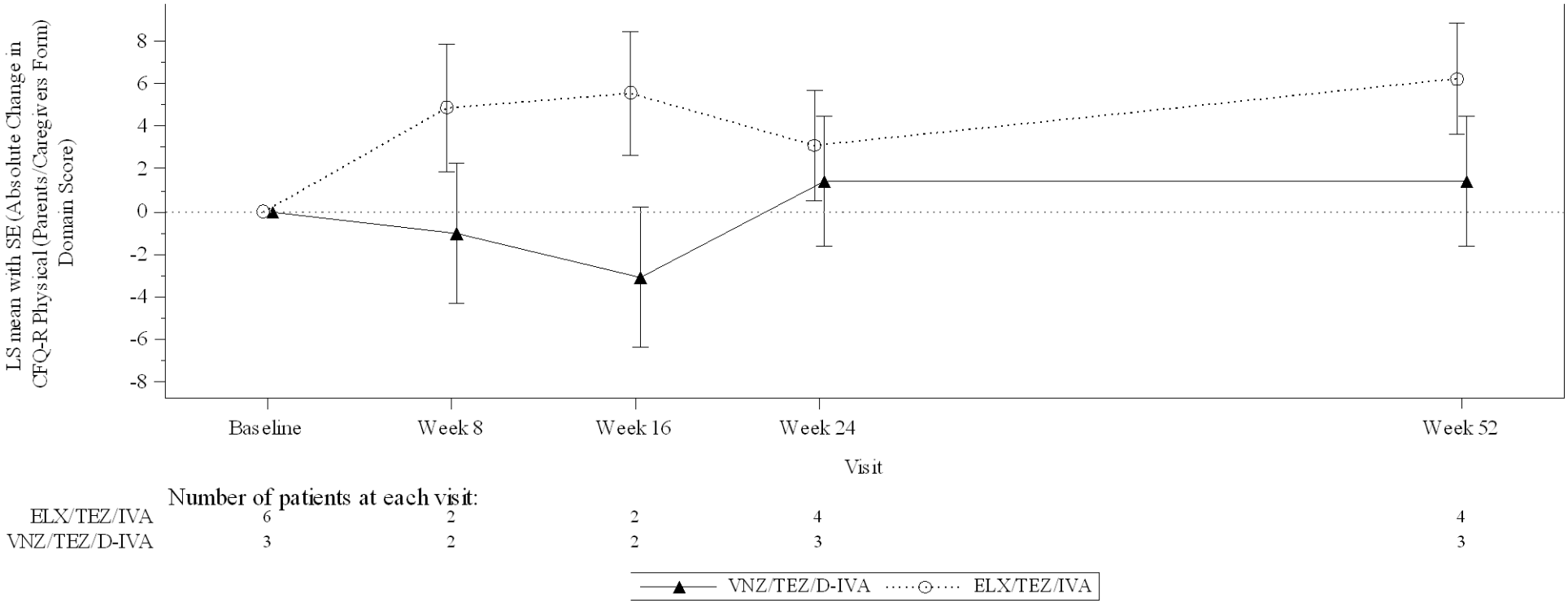

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)
Sex = Female

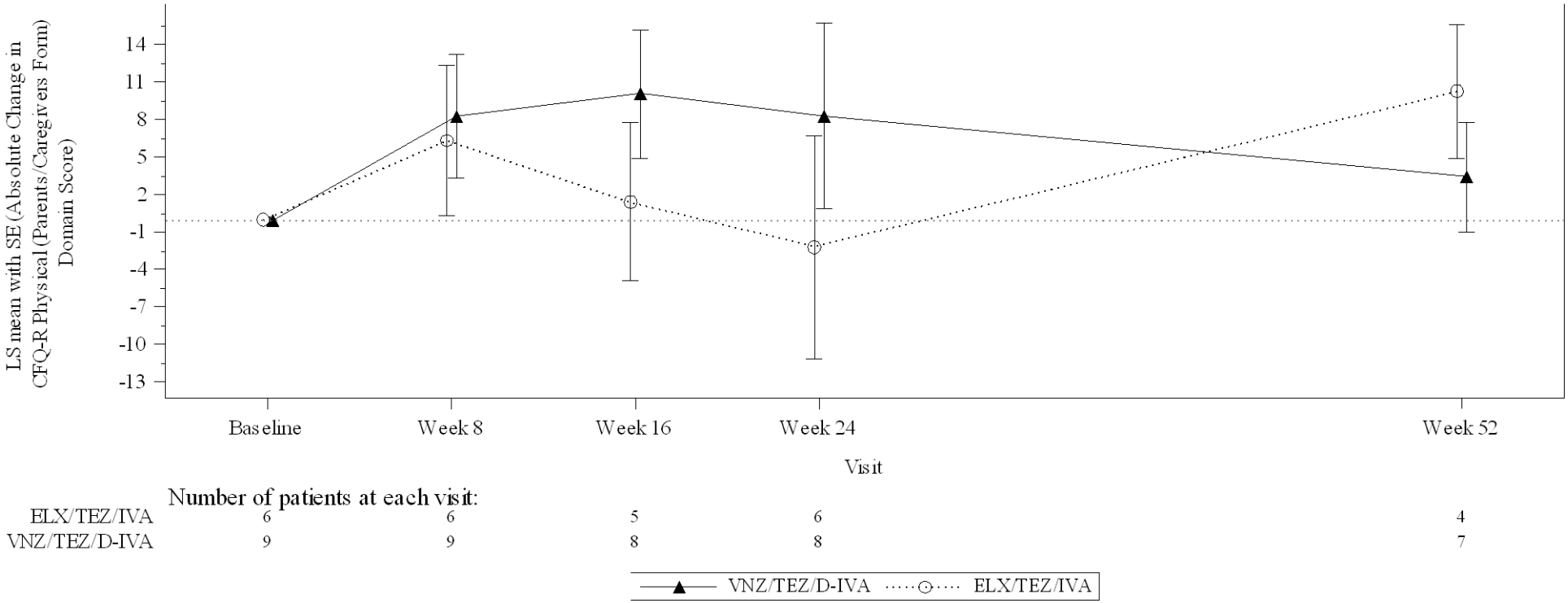

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)
ppFEV$_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

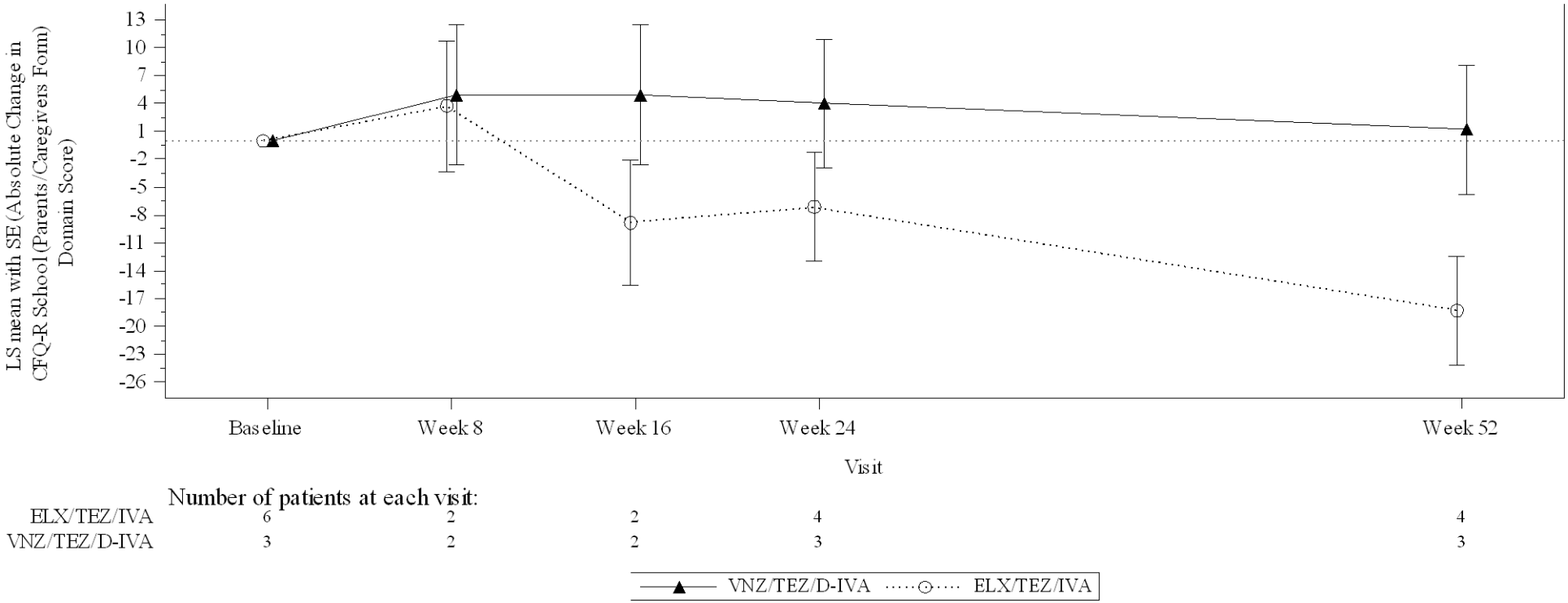
Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)
Sex = Male

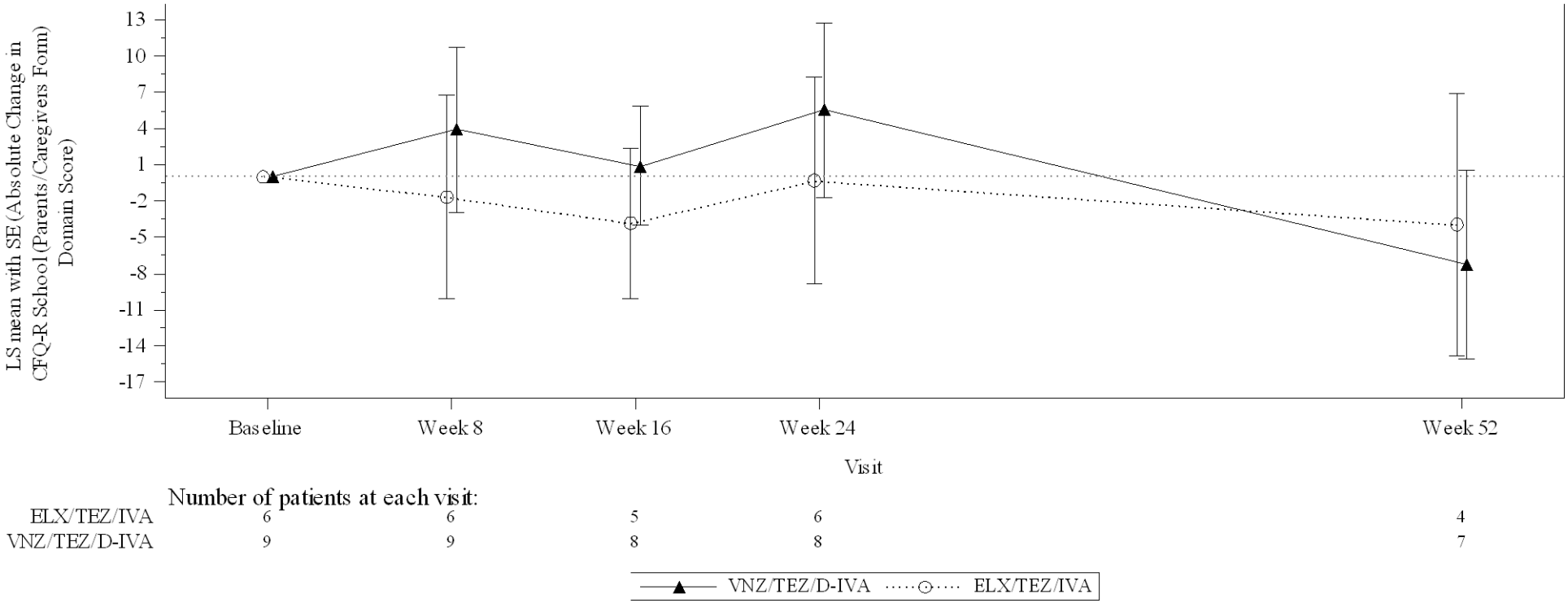


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)
Sex = Female



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- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)
ppFEV$_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

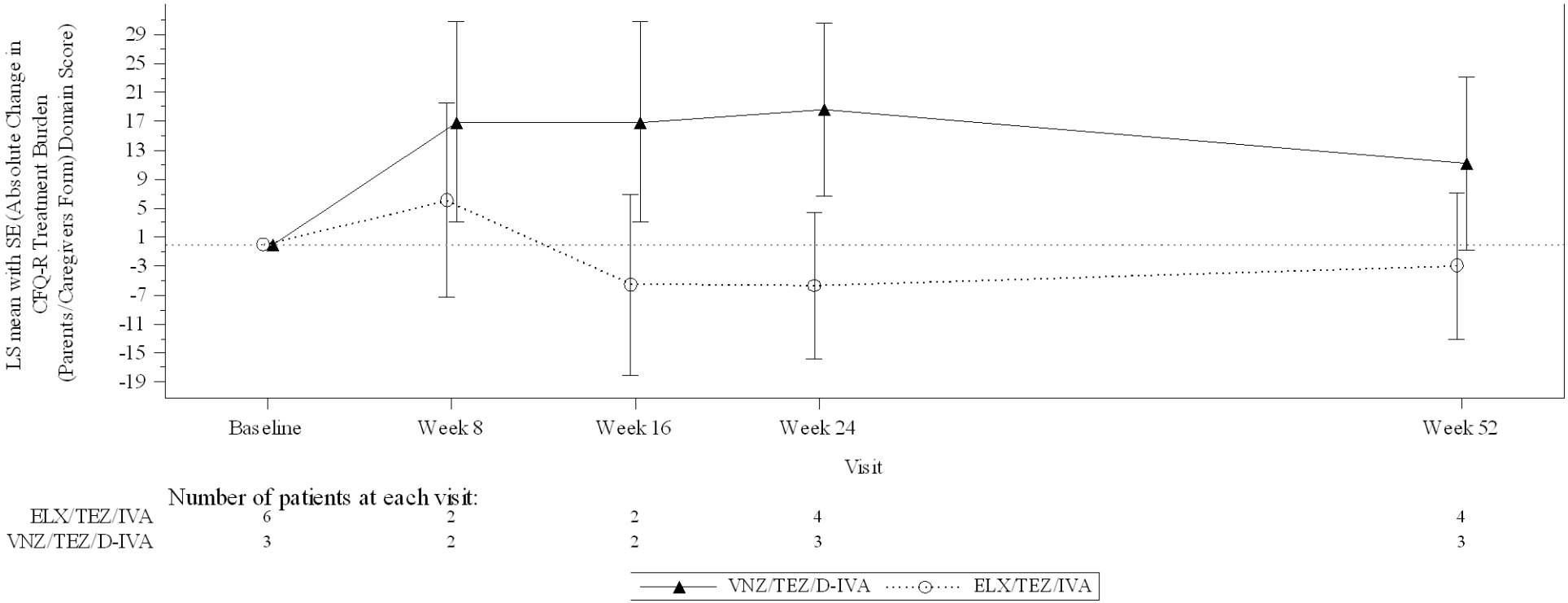

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

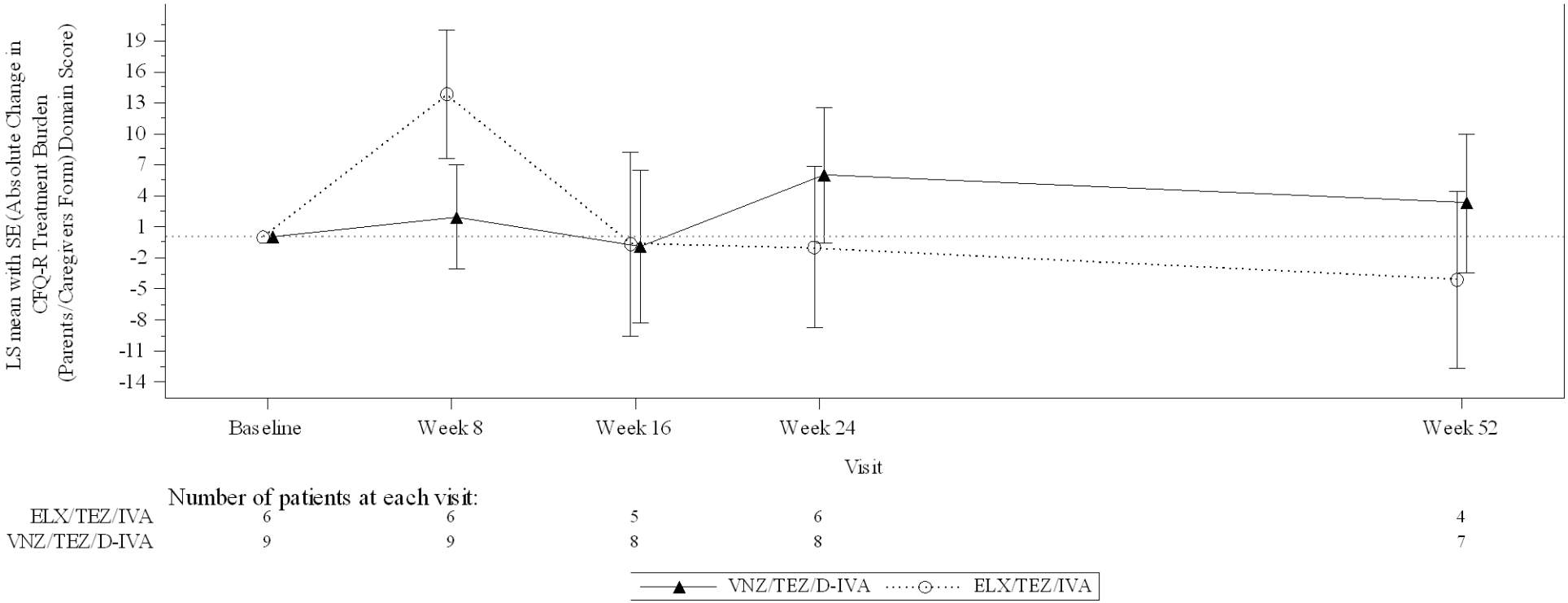

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)
ppFEV$_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)
Sex = Male

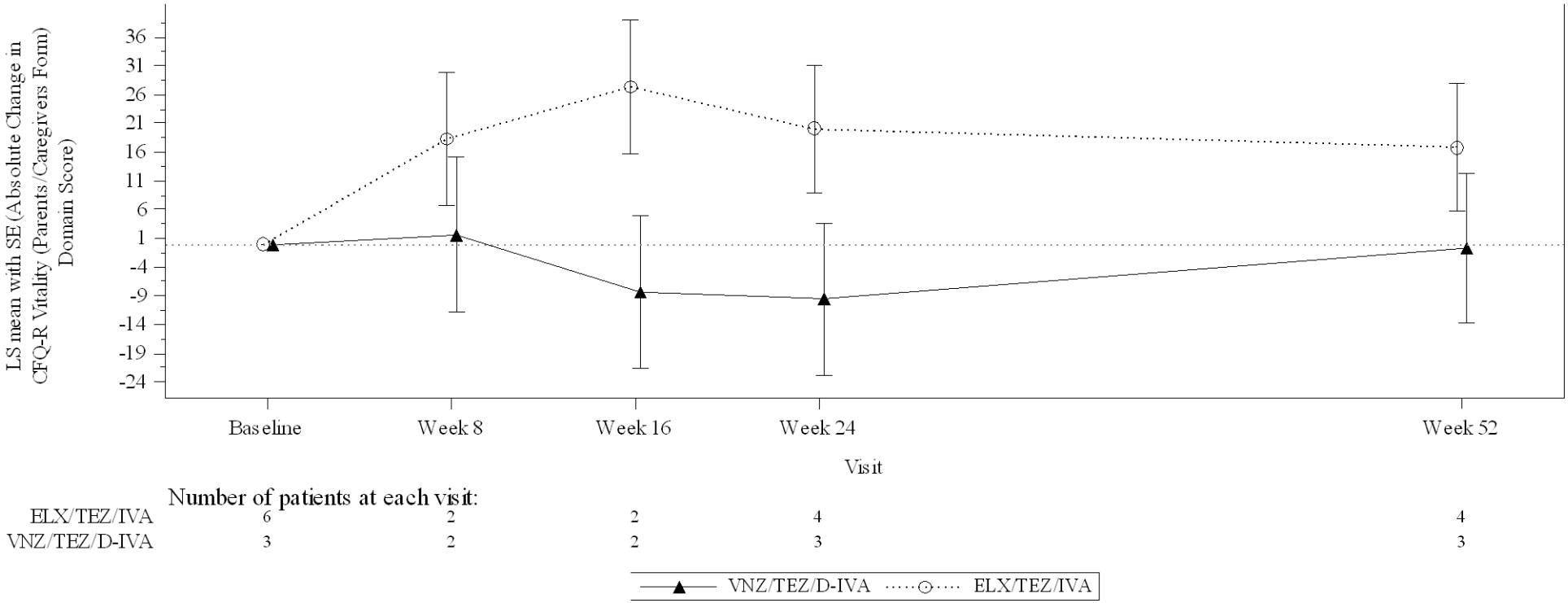

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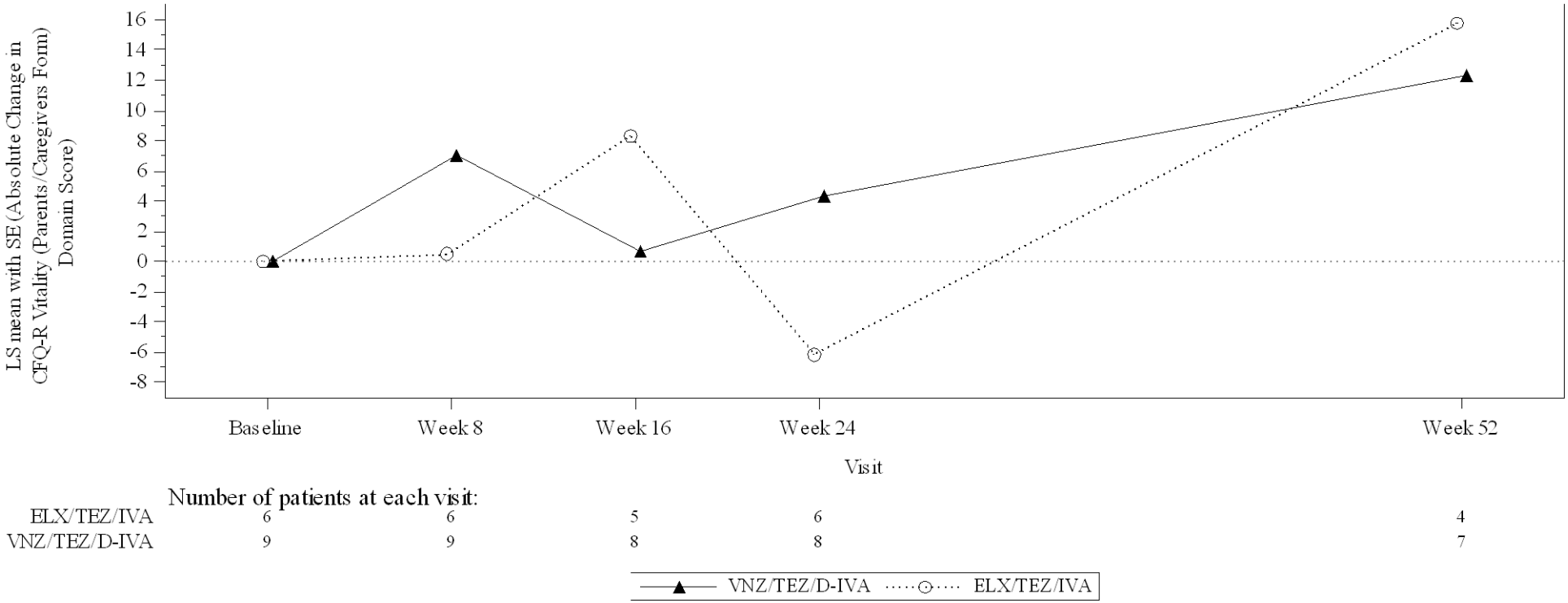
Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)
Sex = Female



Number of patients at each visit:

ELX/TEZ/IVA	6	6	5	6	4
VNZ/TEZ/D-IVA	9	9	8	8	7

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

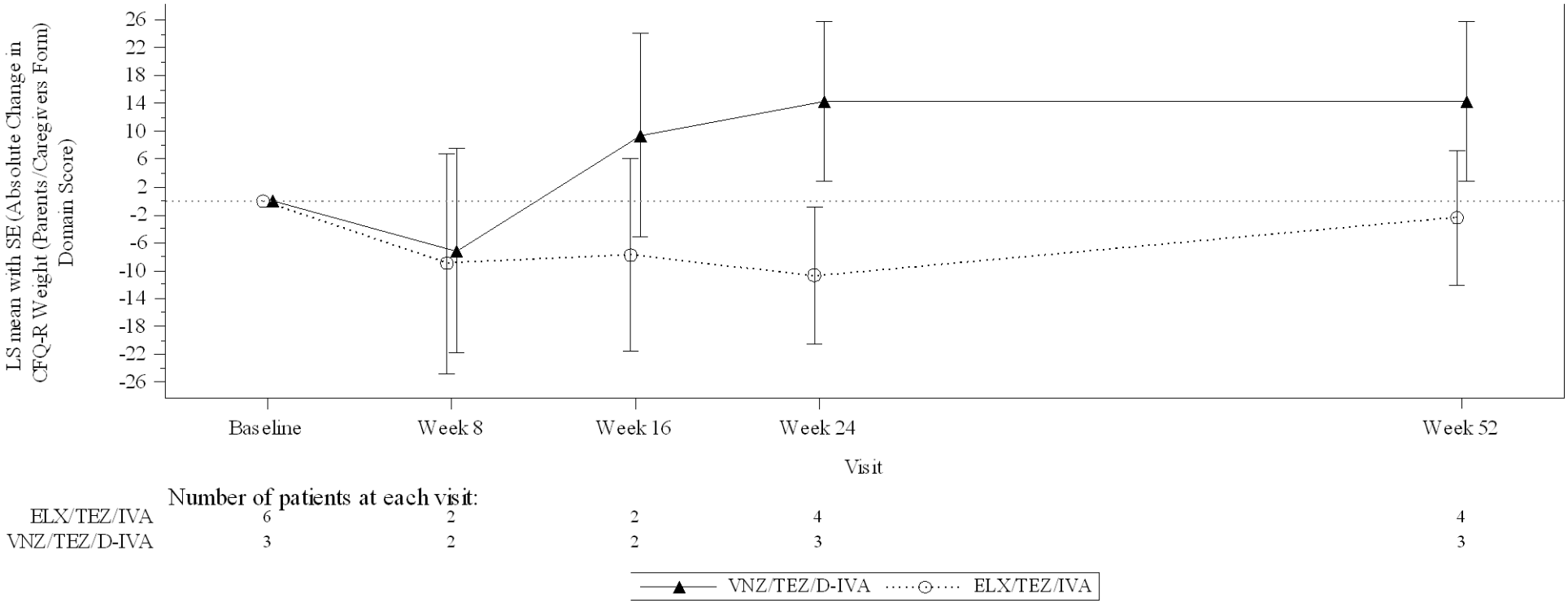
Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)
Sex = Male

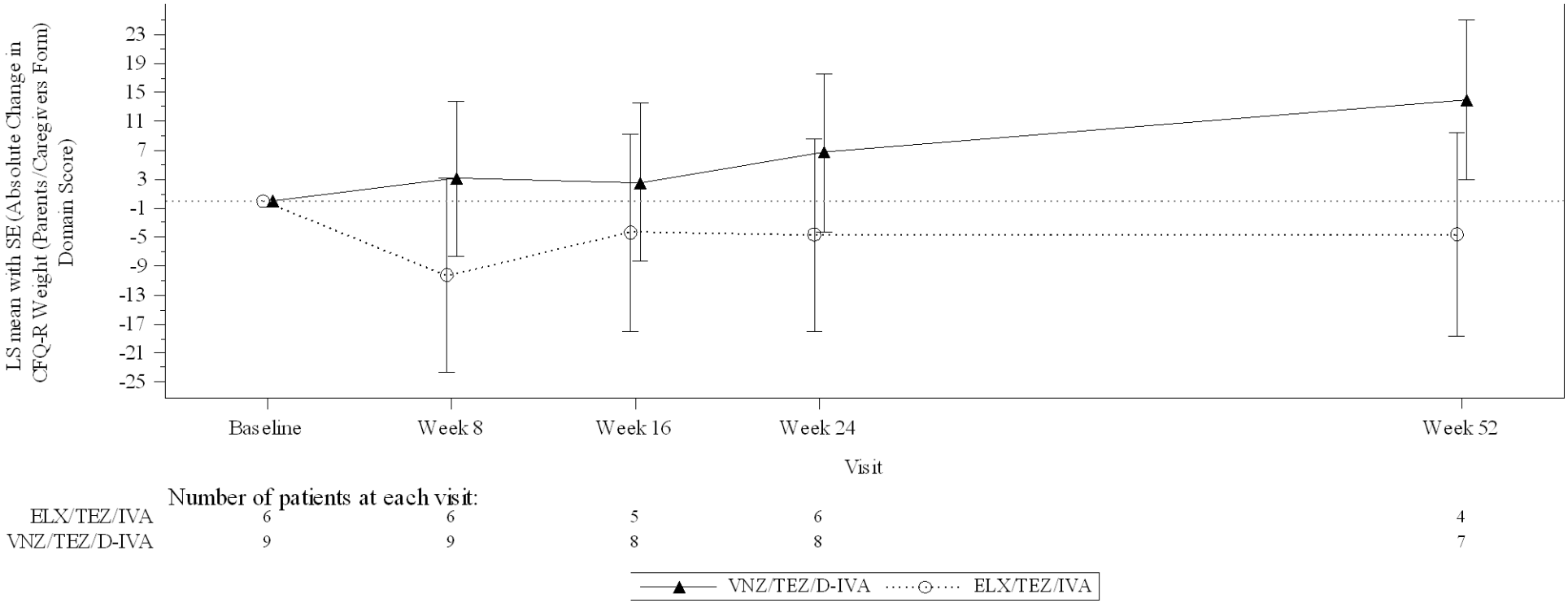


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

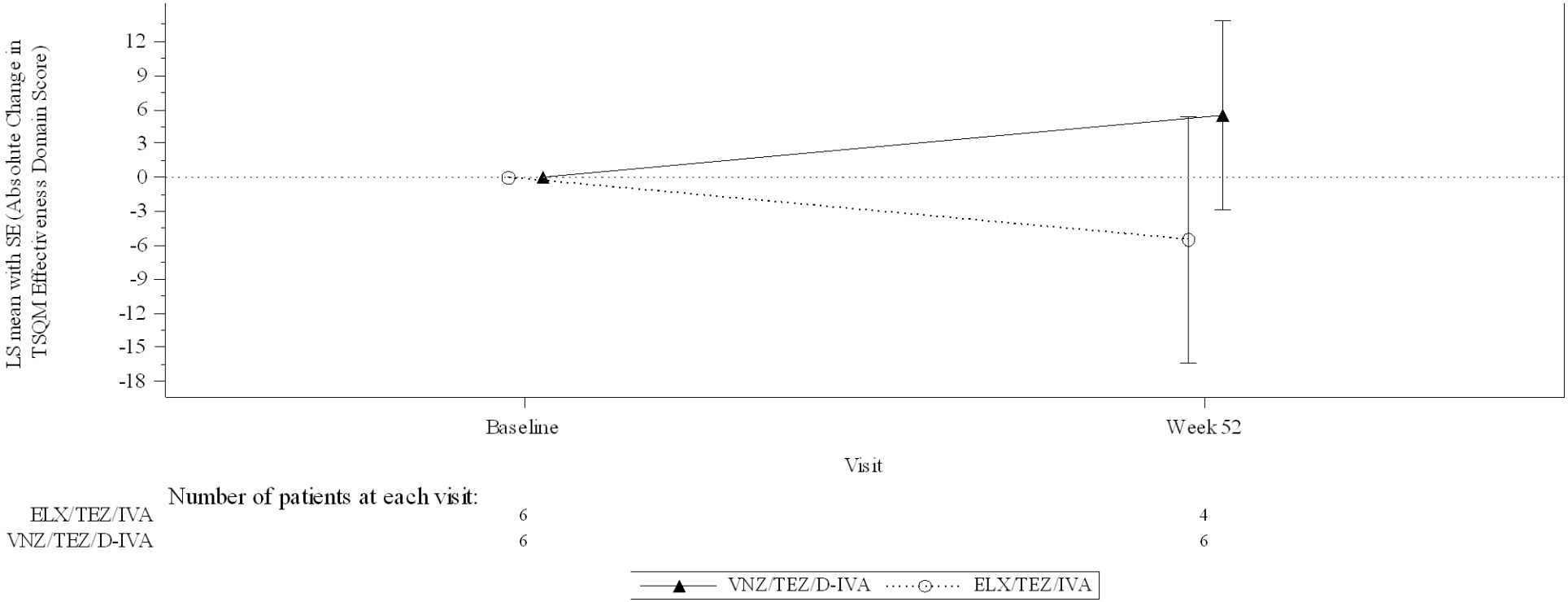
Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-cg-52wks-sub-103.sas Creation: 11JAN2025 16:08

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
ppFEV$_1$ at baseline <70 %

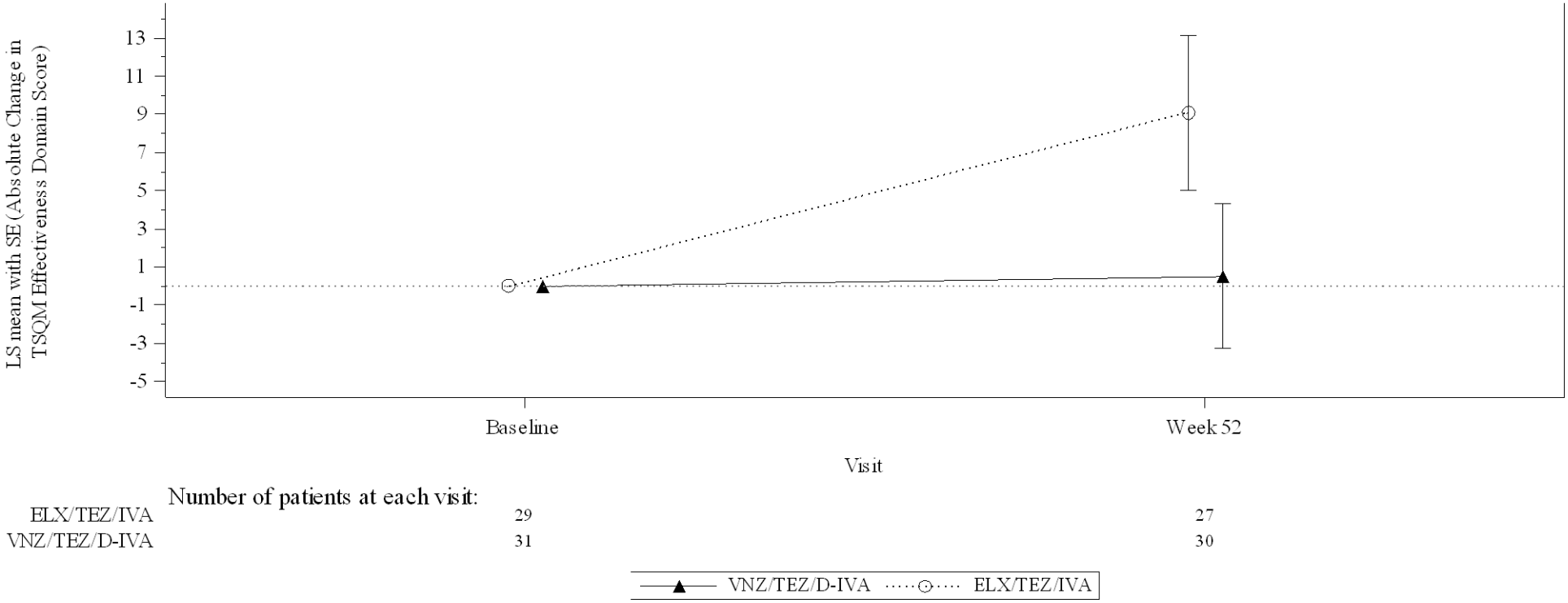


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
ppFEV$_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Age at screening <18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Age at screening ≥18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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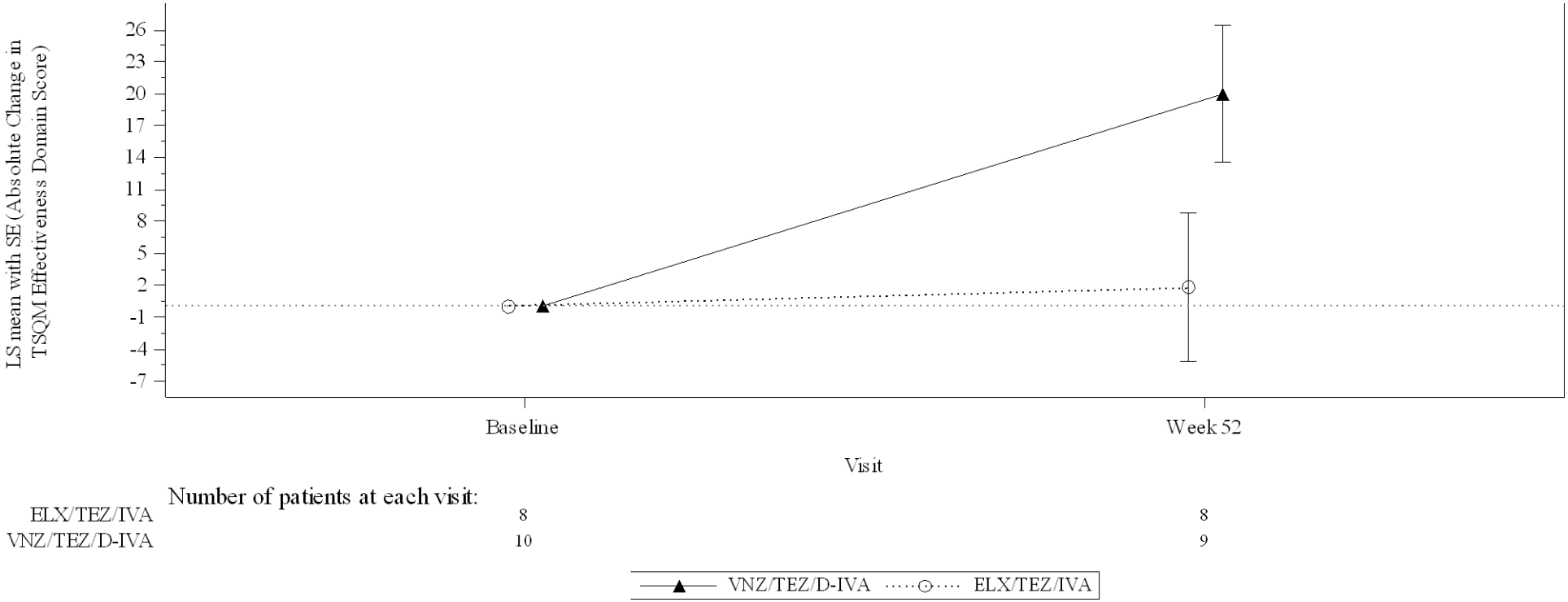
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
SwCl at baseline <30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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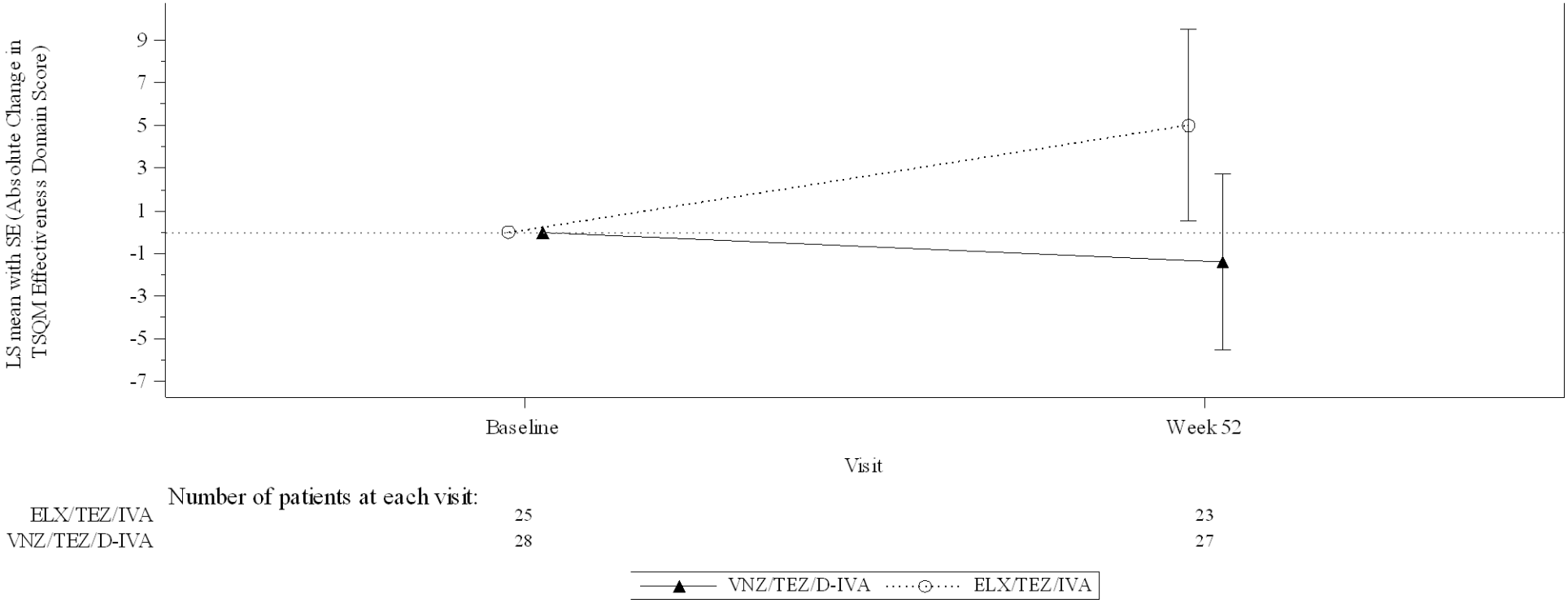
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
SwCl at baseline ≥30 mmol/L

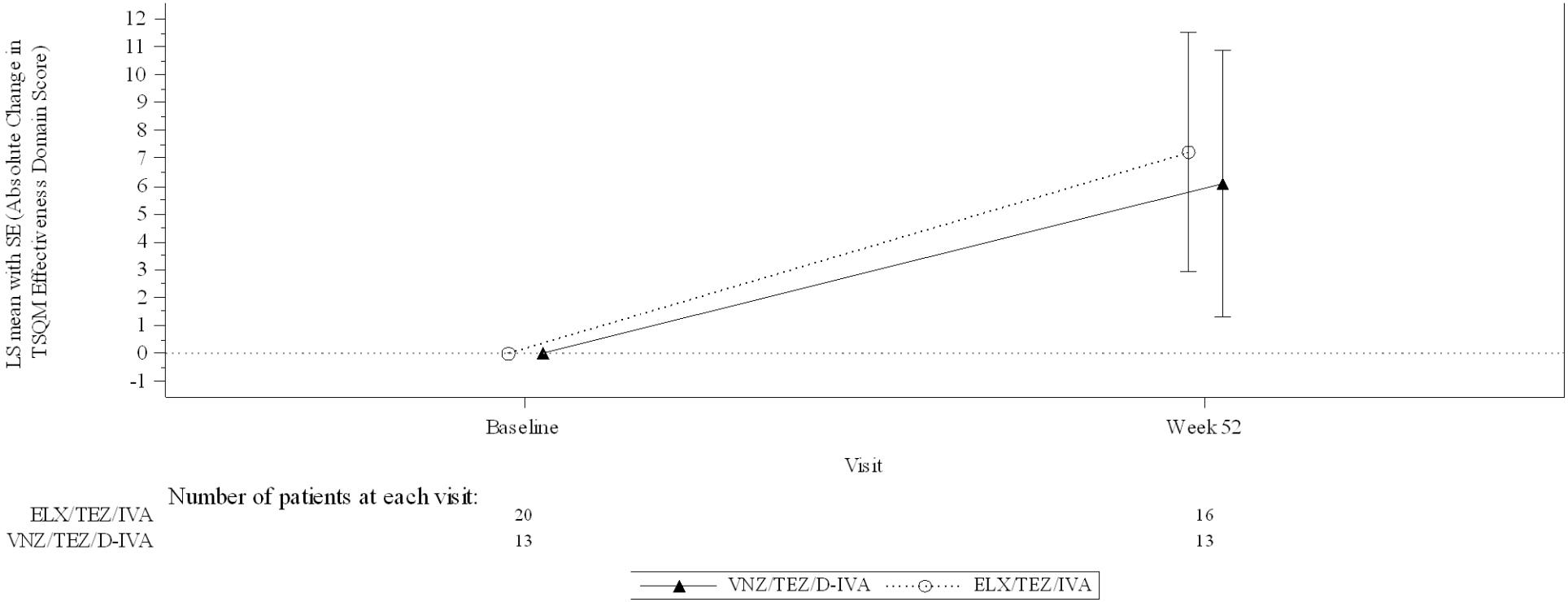


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Male

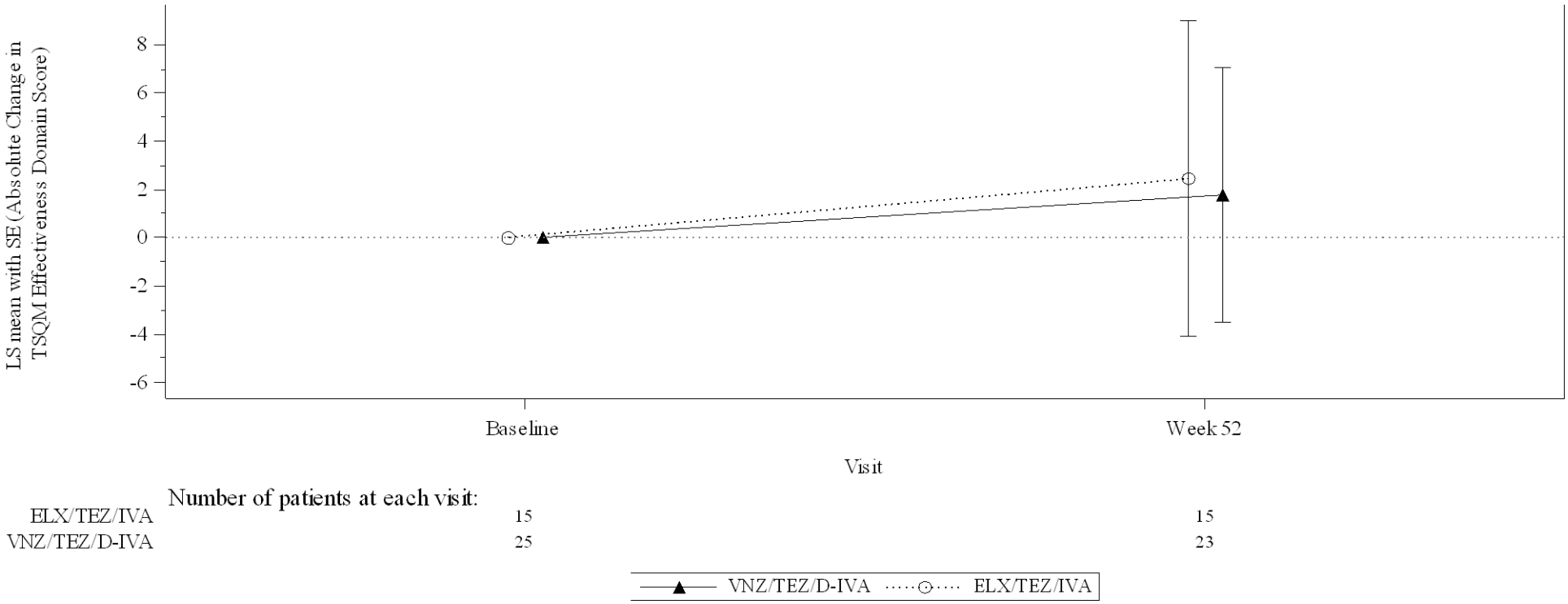


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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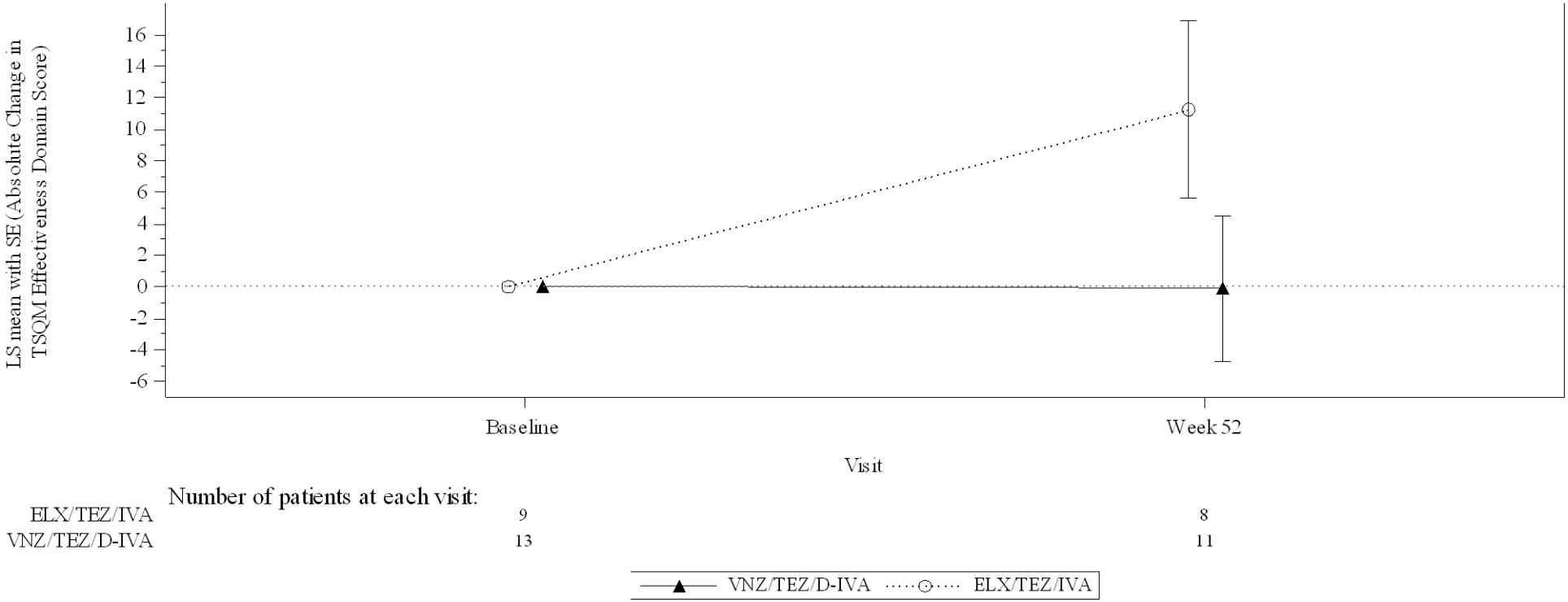
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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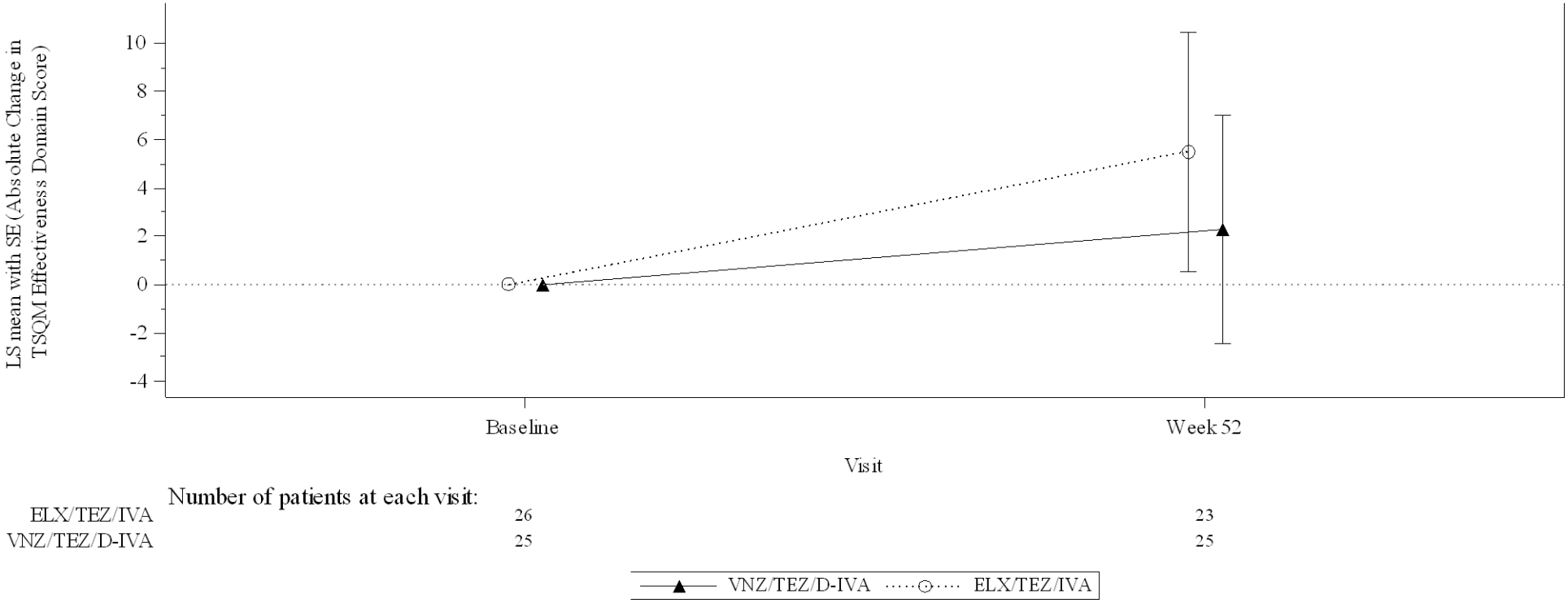
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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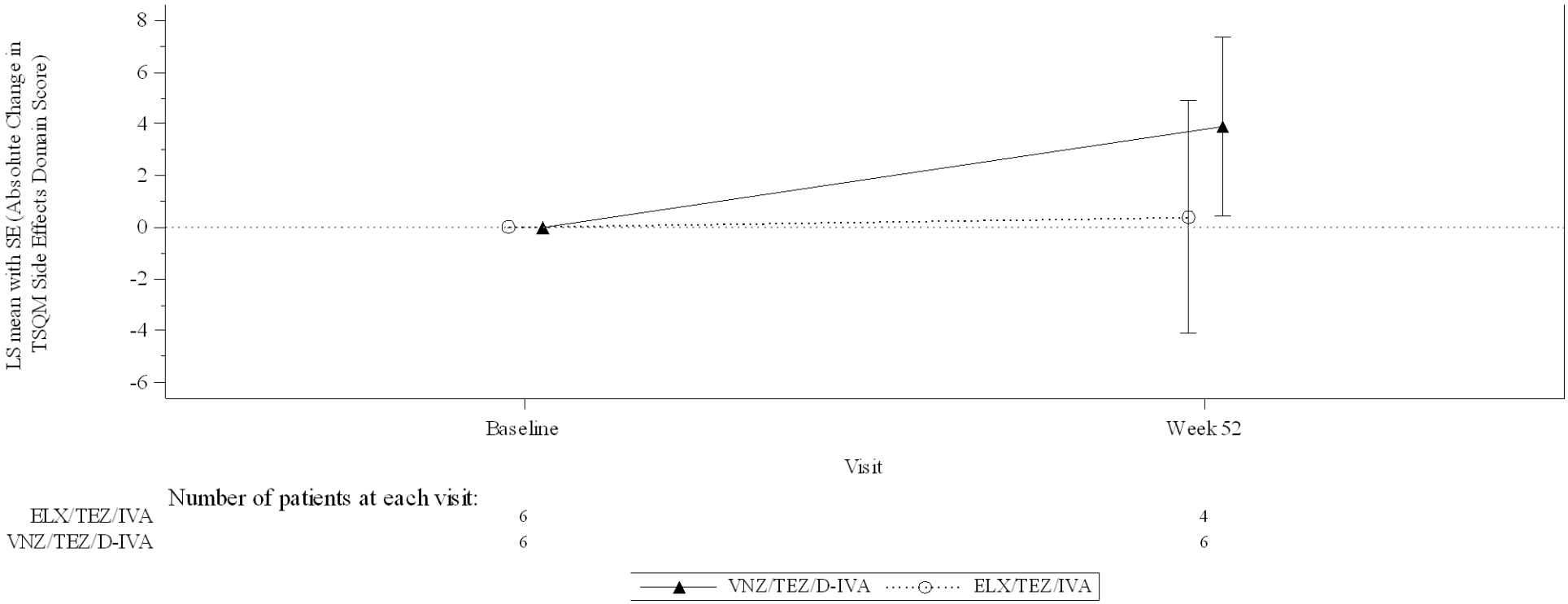
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
ppFEV$_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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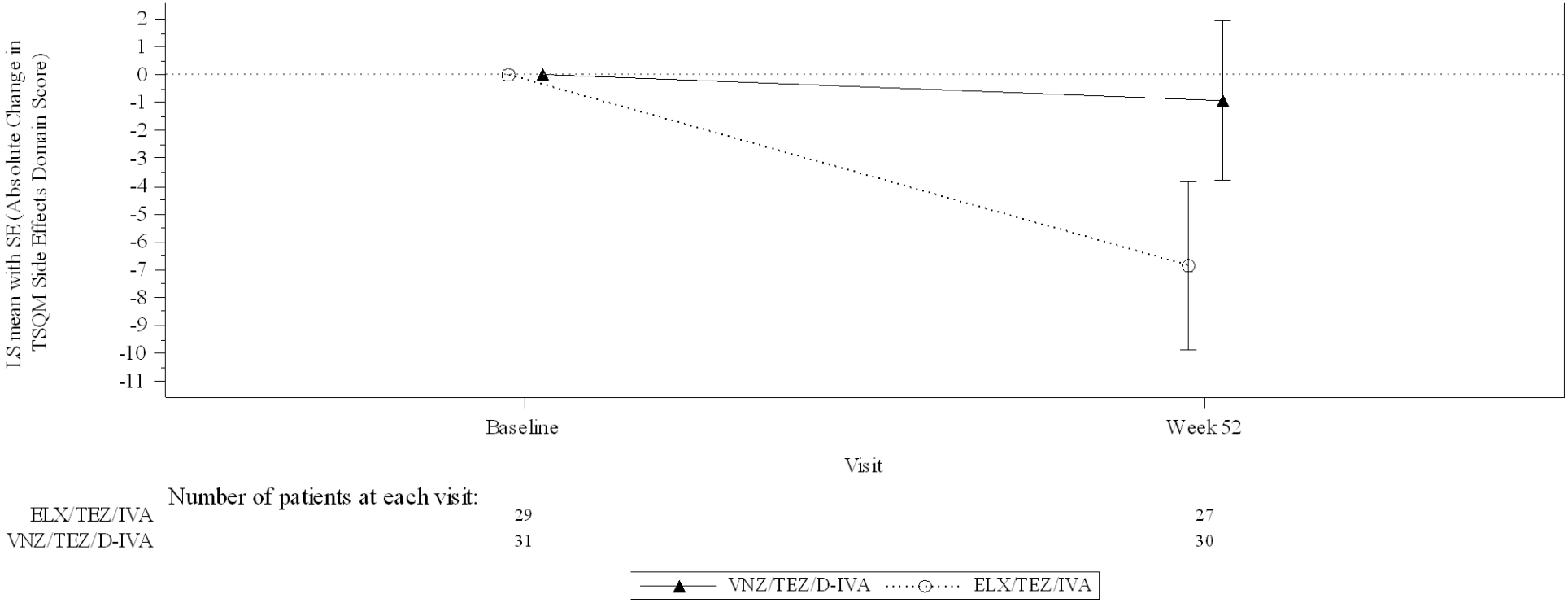
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
ppFEV$_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Age at screening <18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Age at screening ≥18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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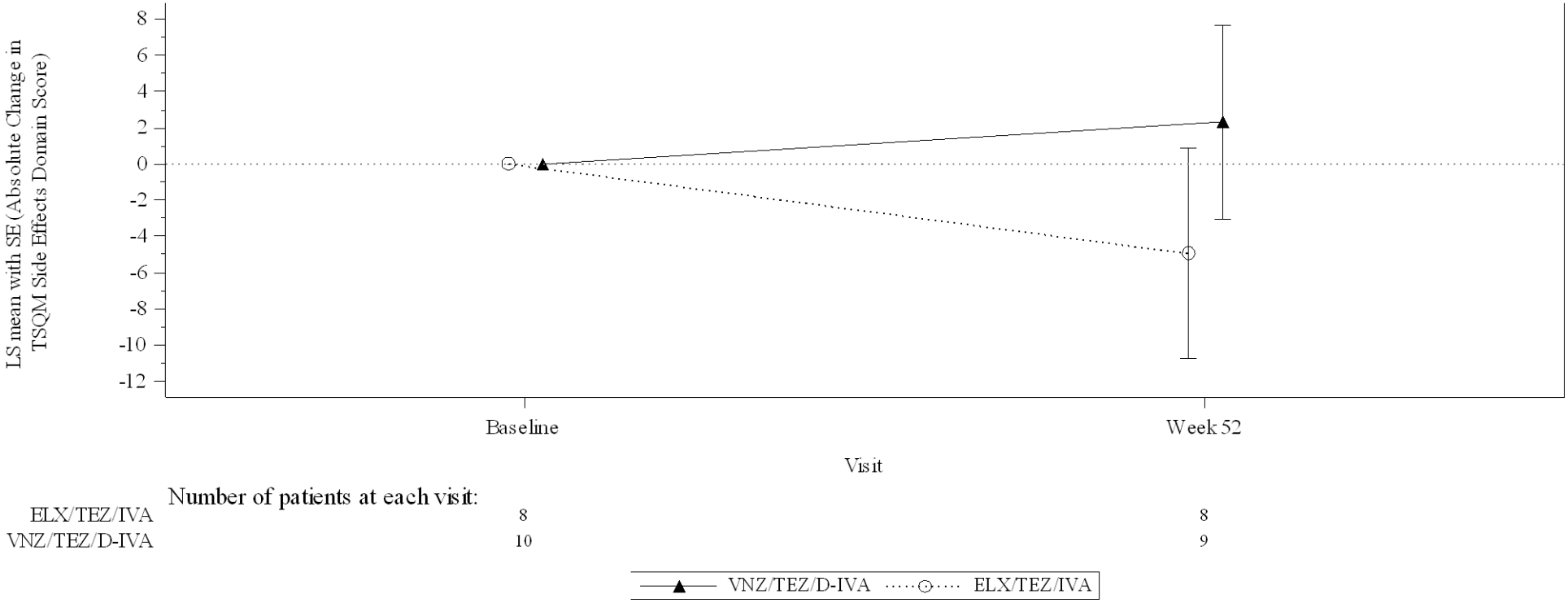
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
SwCl at baseline <30 mmol/L

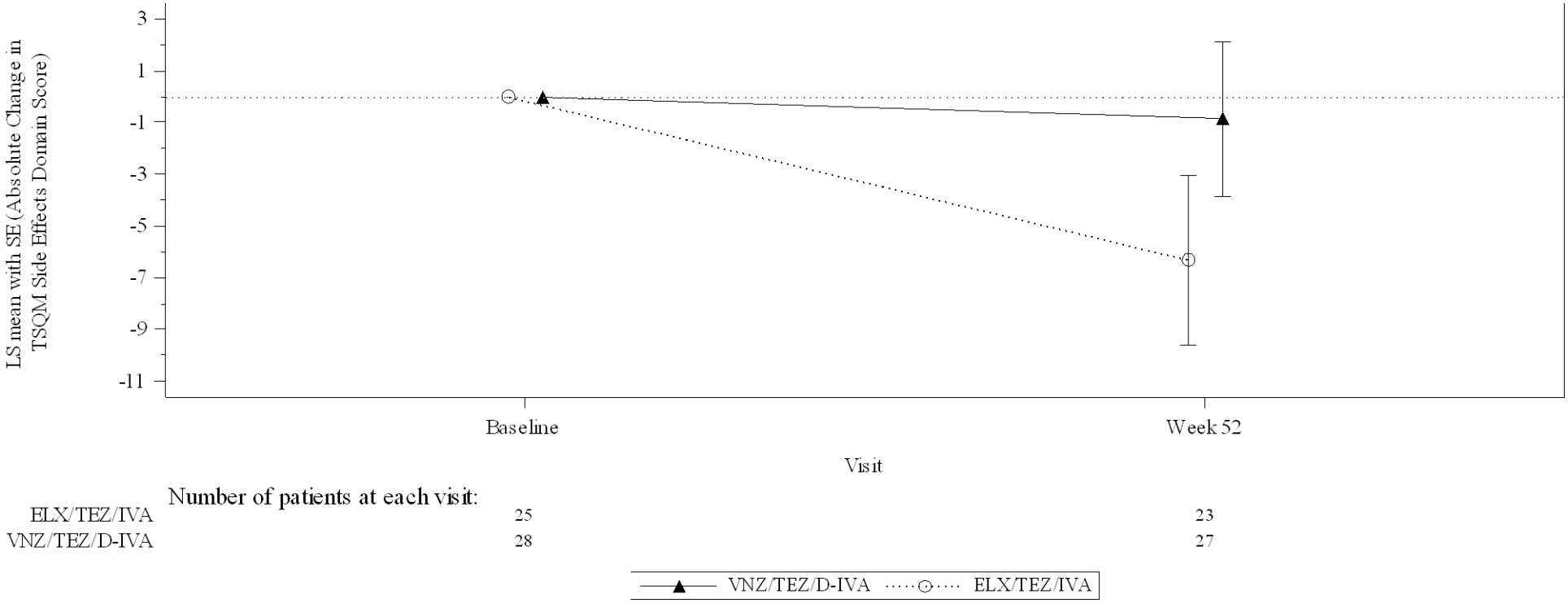


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
SwCl at baseline ≥30 mmol/L

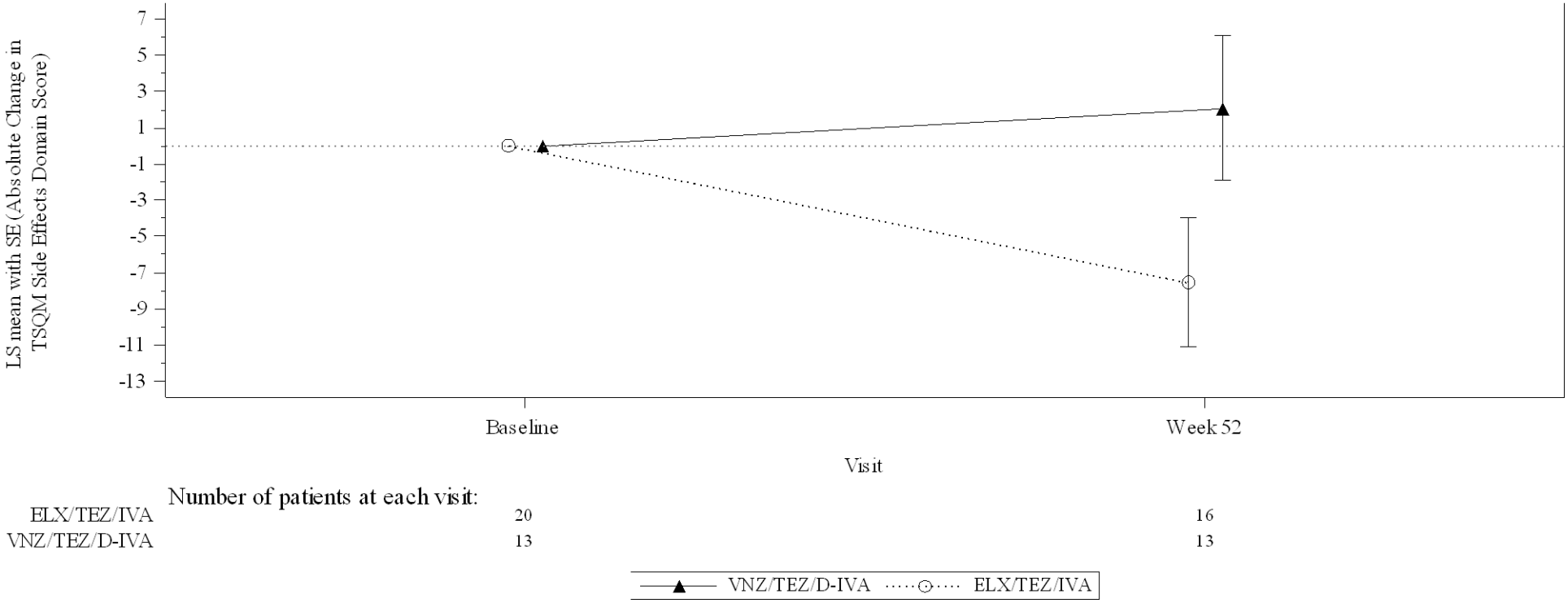


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Male

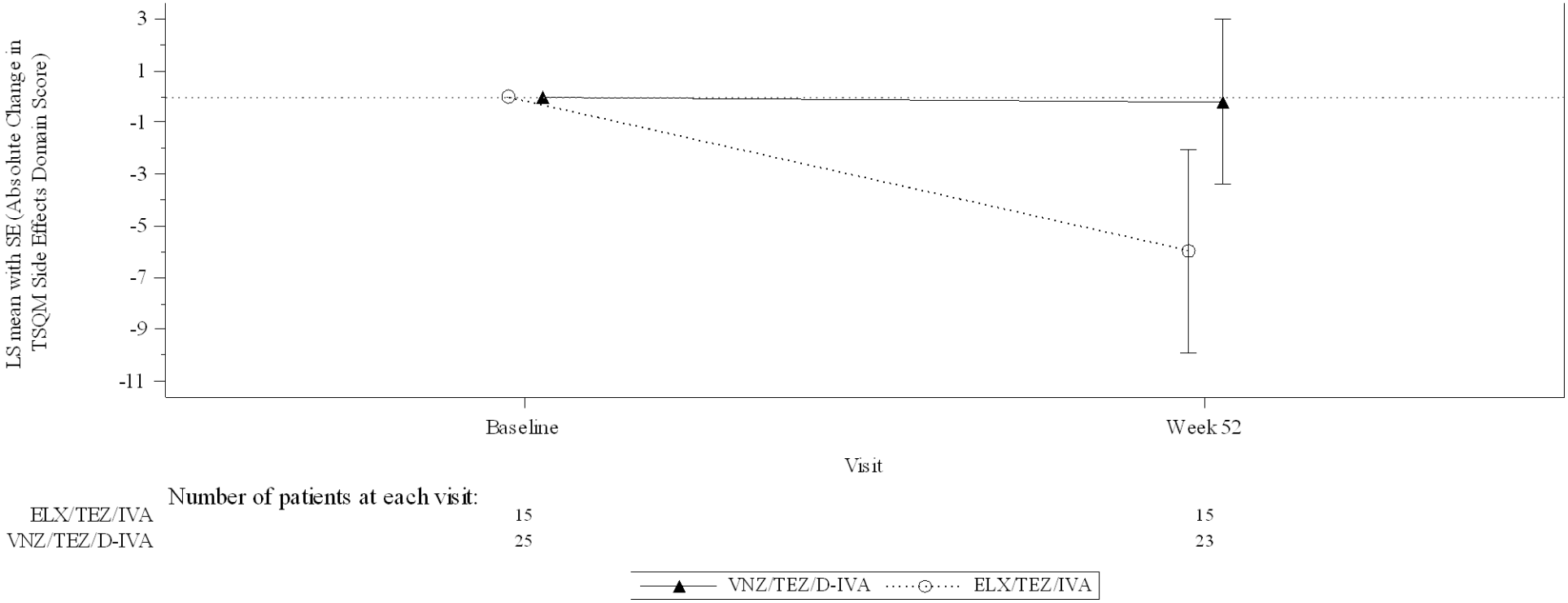


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Female

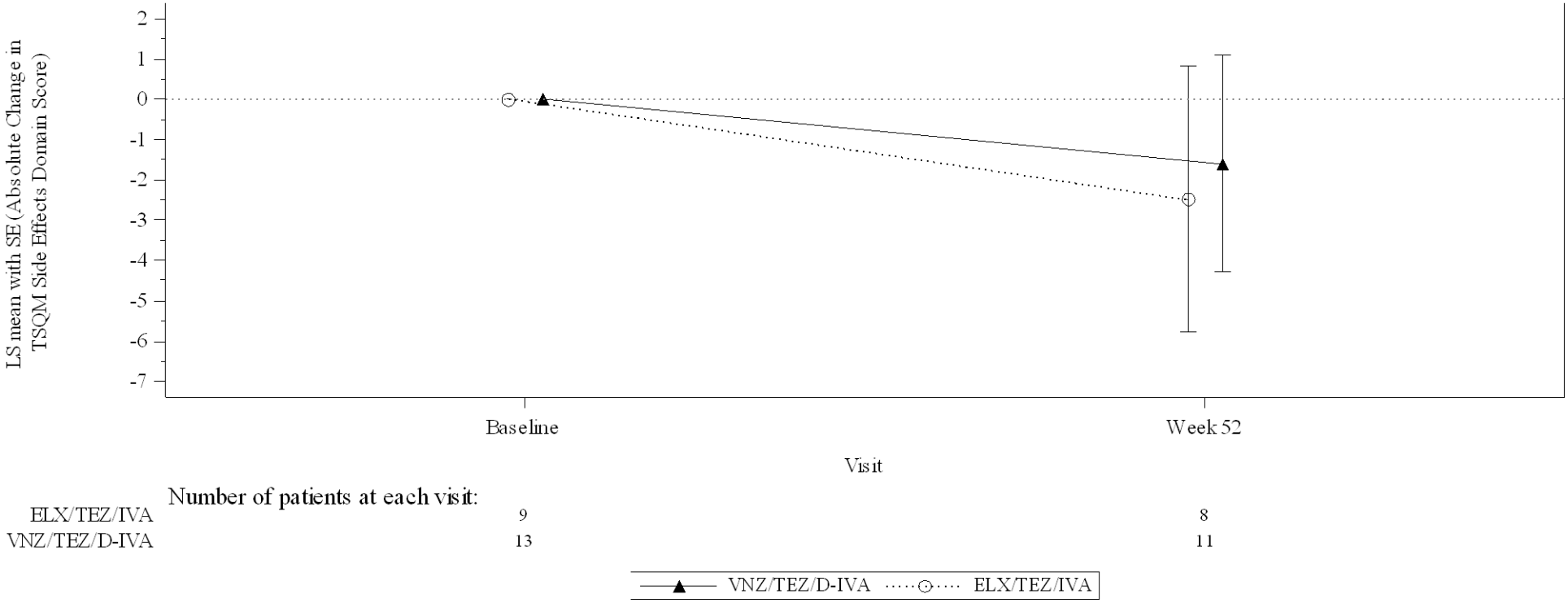


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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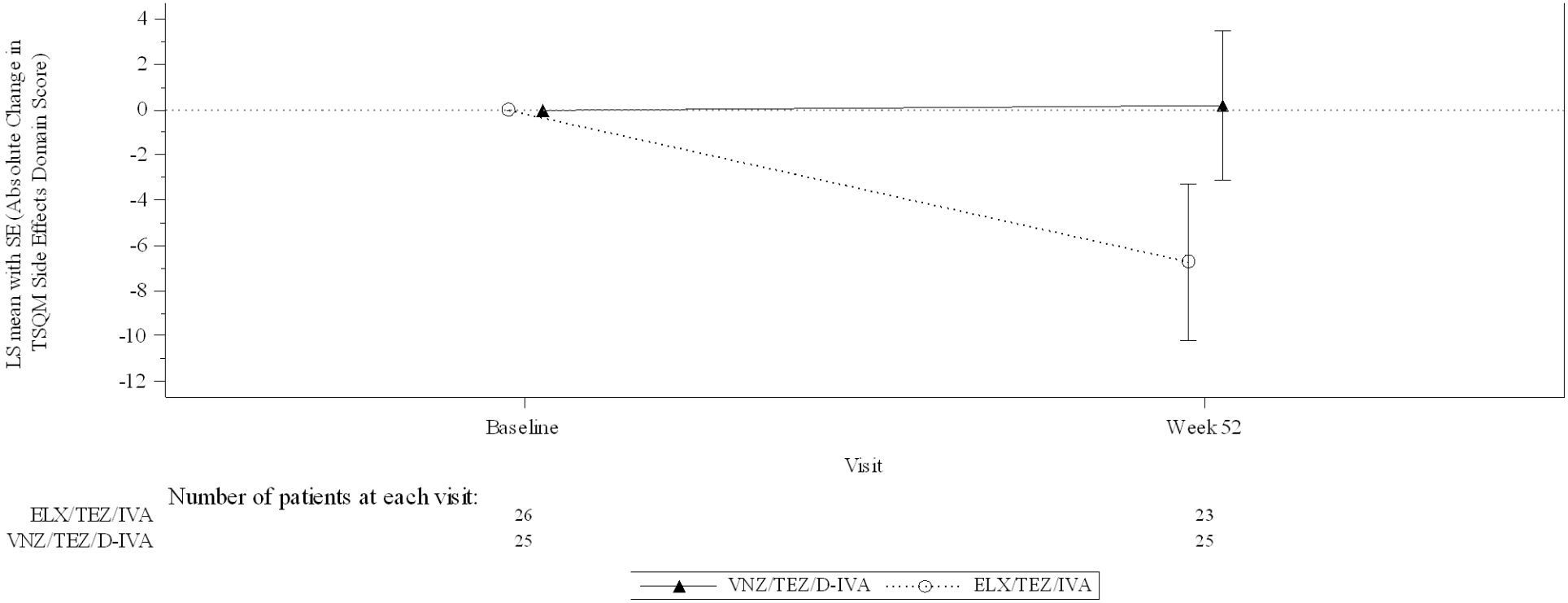
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = Rest of World



Number of patients at each visit:

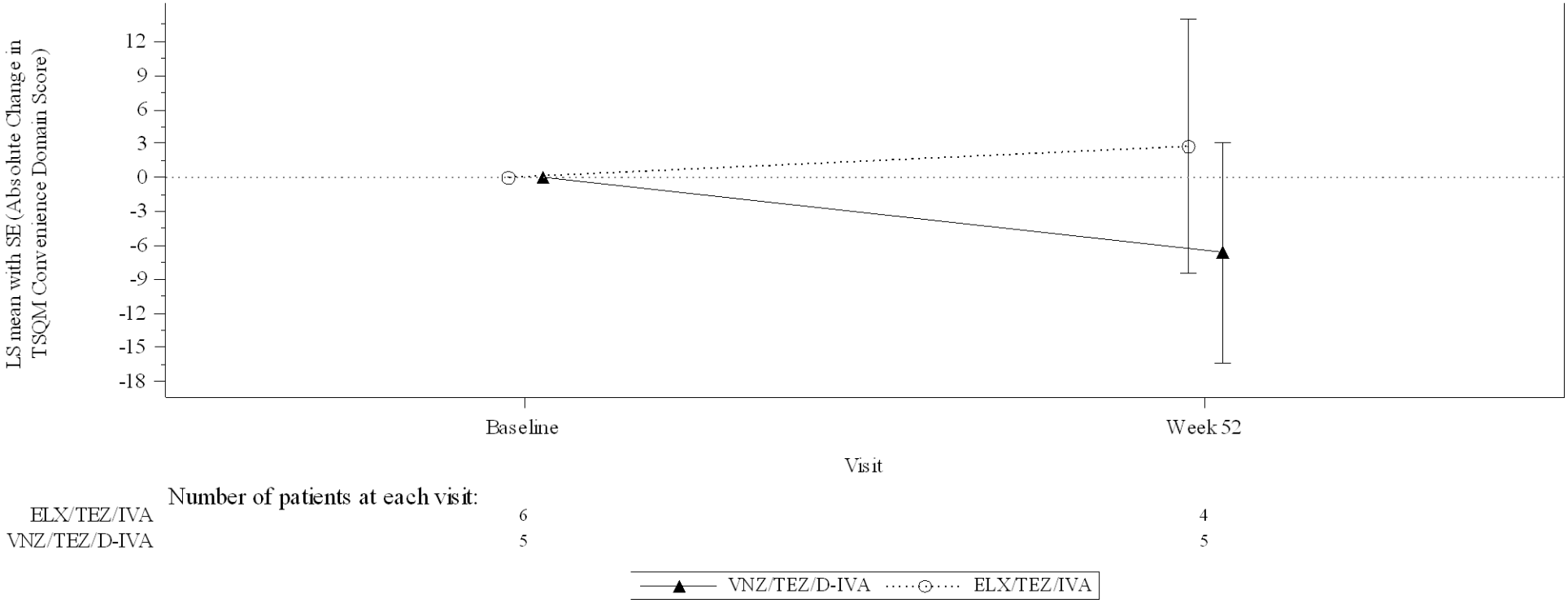
	Baseline	Week 52
ELX/TEZ/IVA	26	23
VNZ/TEZ/D-IVA	25	25

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
ppFEV$_1$ at baseline <70 %

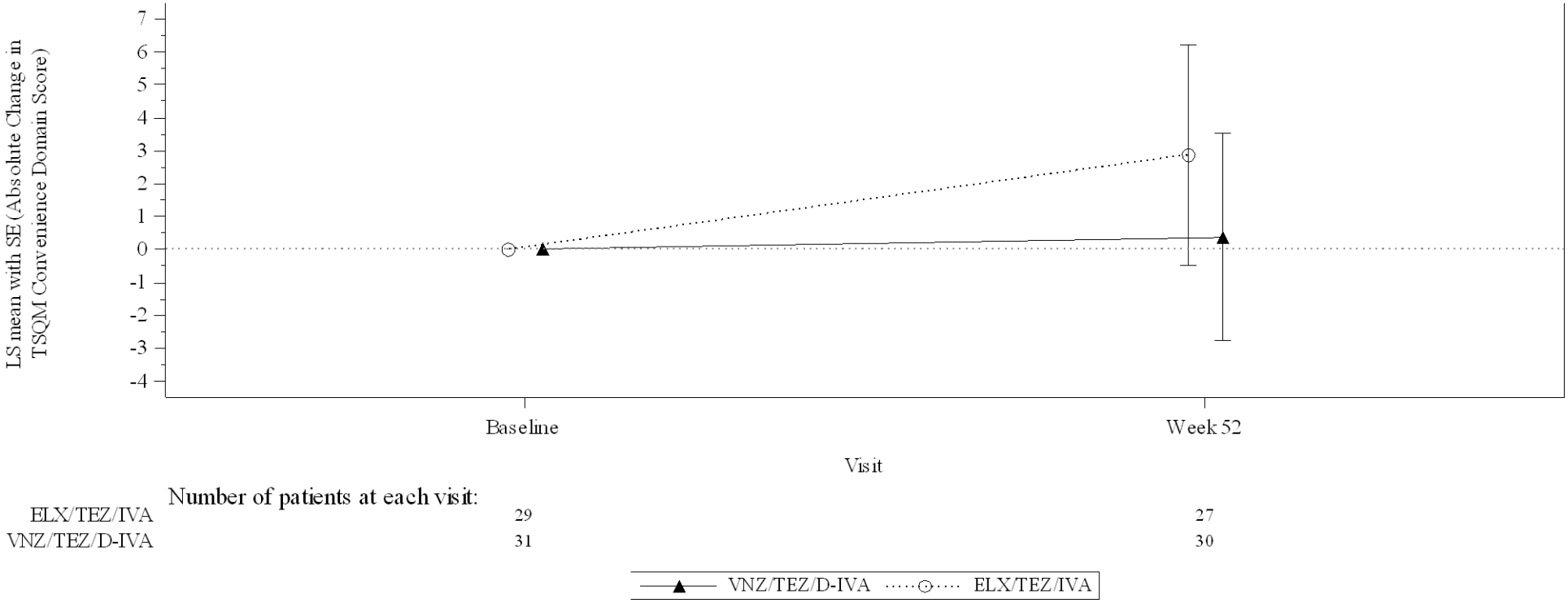


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
ppFEV$_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Age at screening <18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Age at screening ≥18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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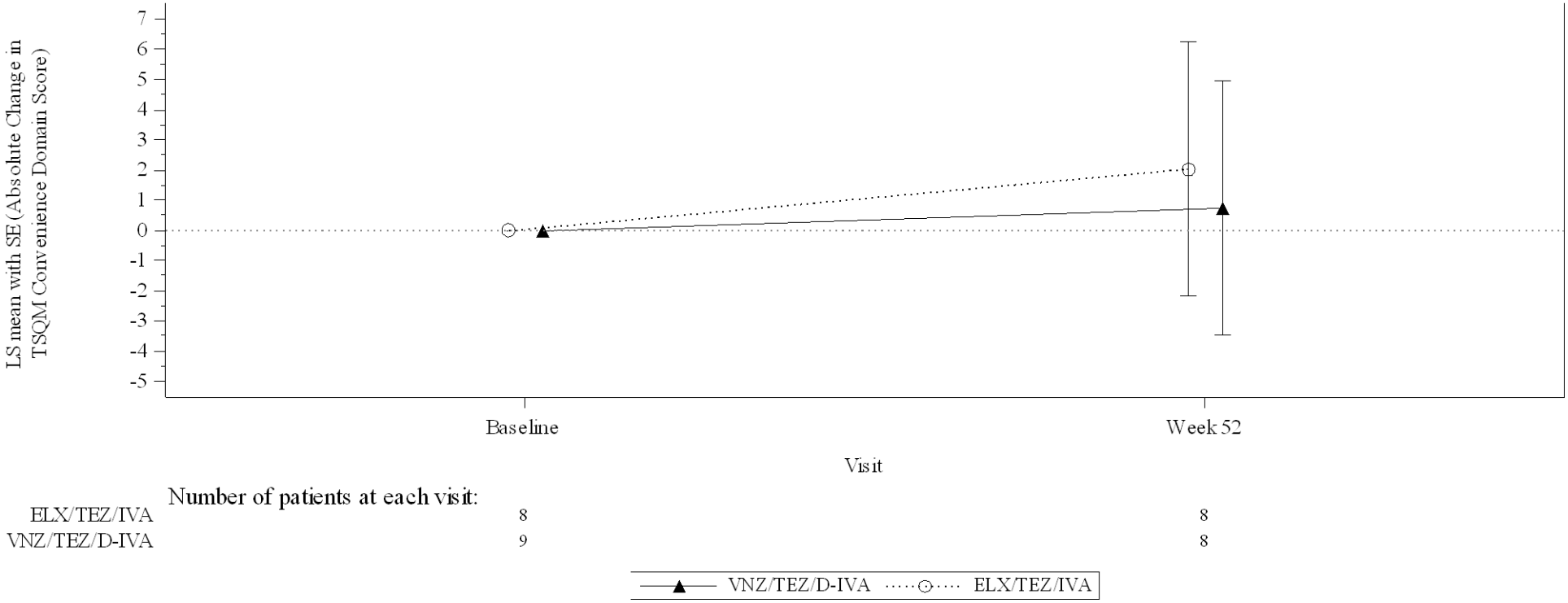
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
SwCl at baseline <30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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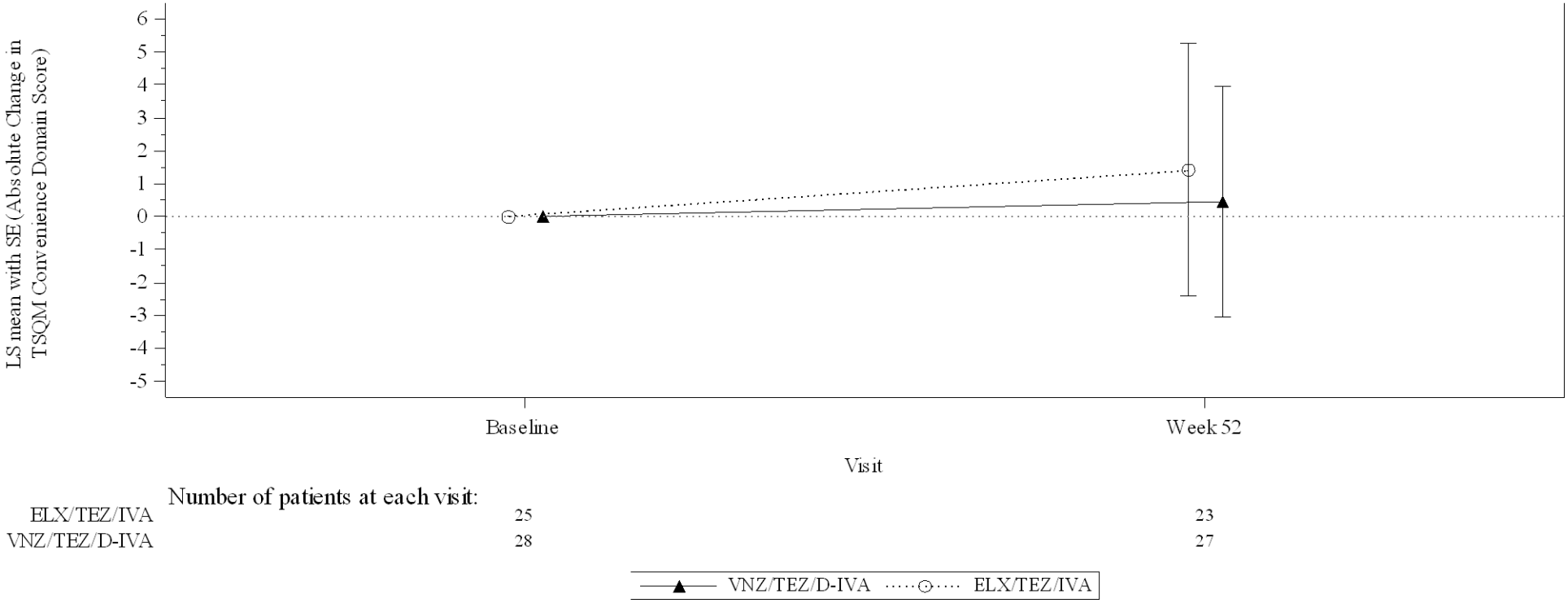
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
SwCl at baseline ≥30 mmol/L



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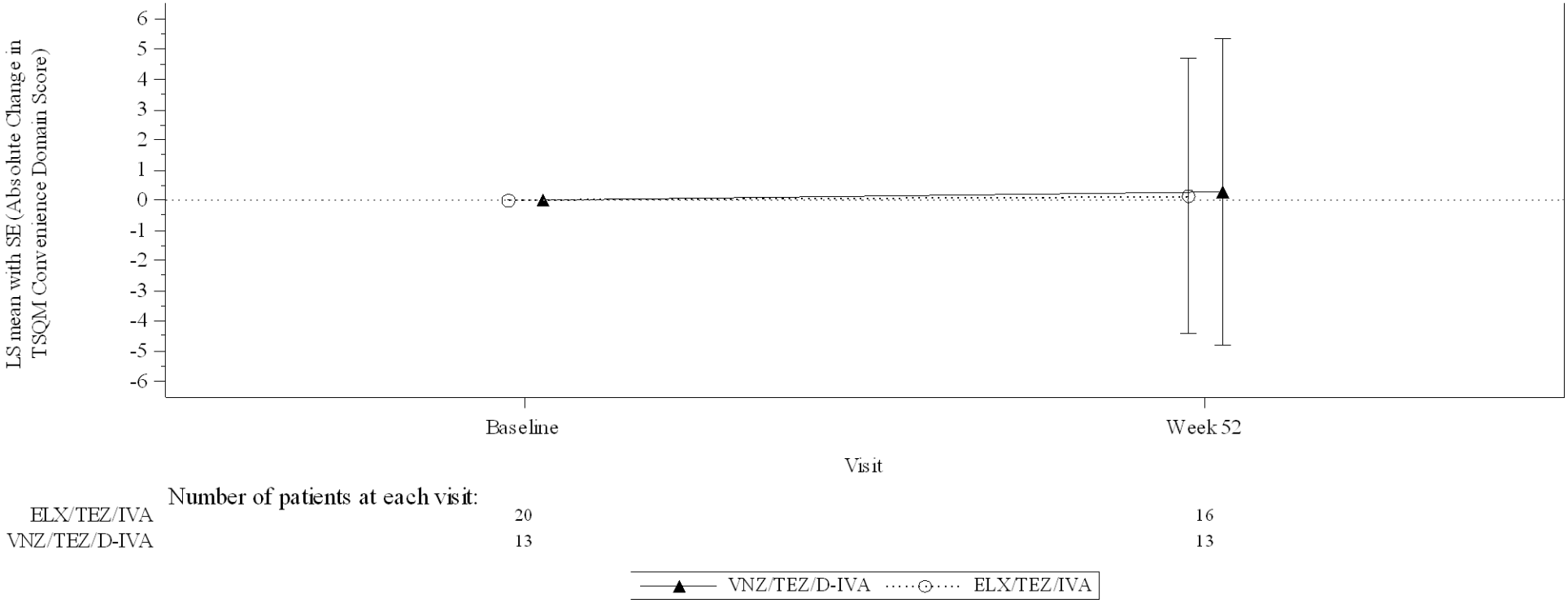
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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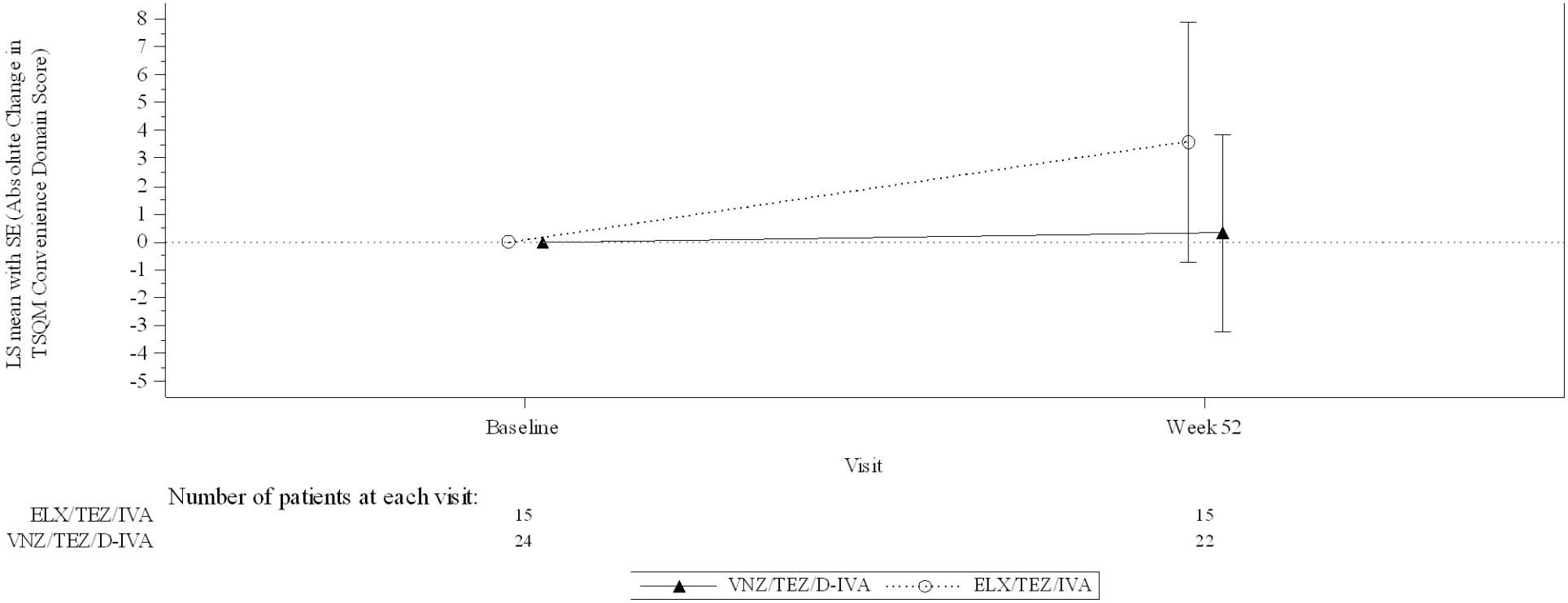
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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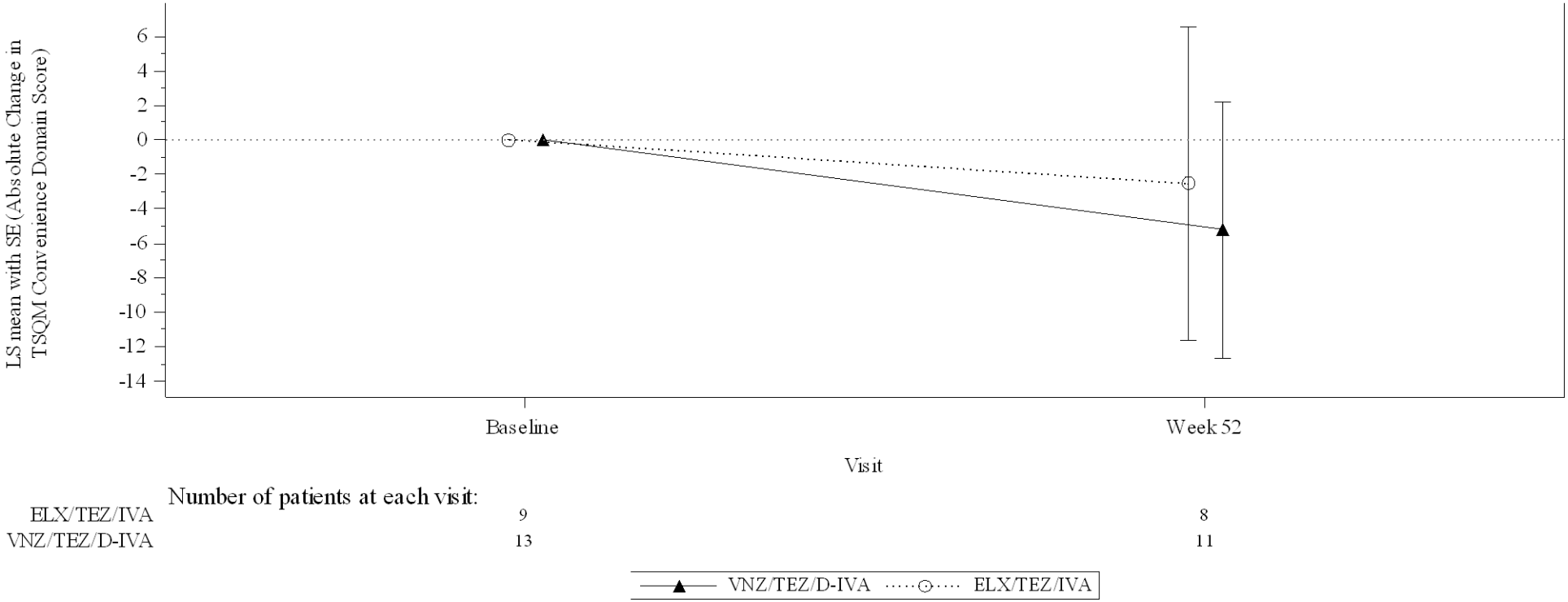
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = North America



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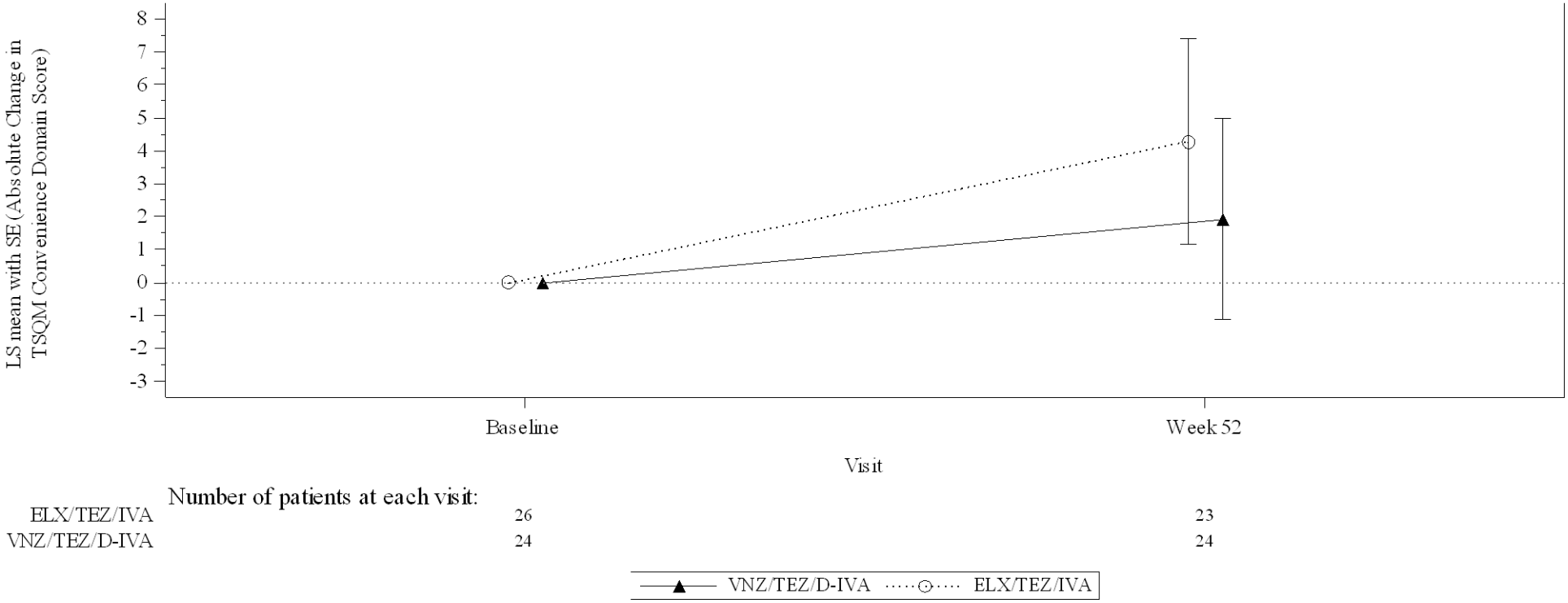
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = Rest of World



Number of patients at each visit:

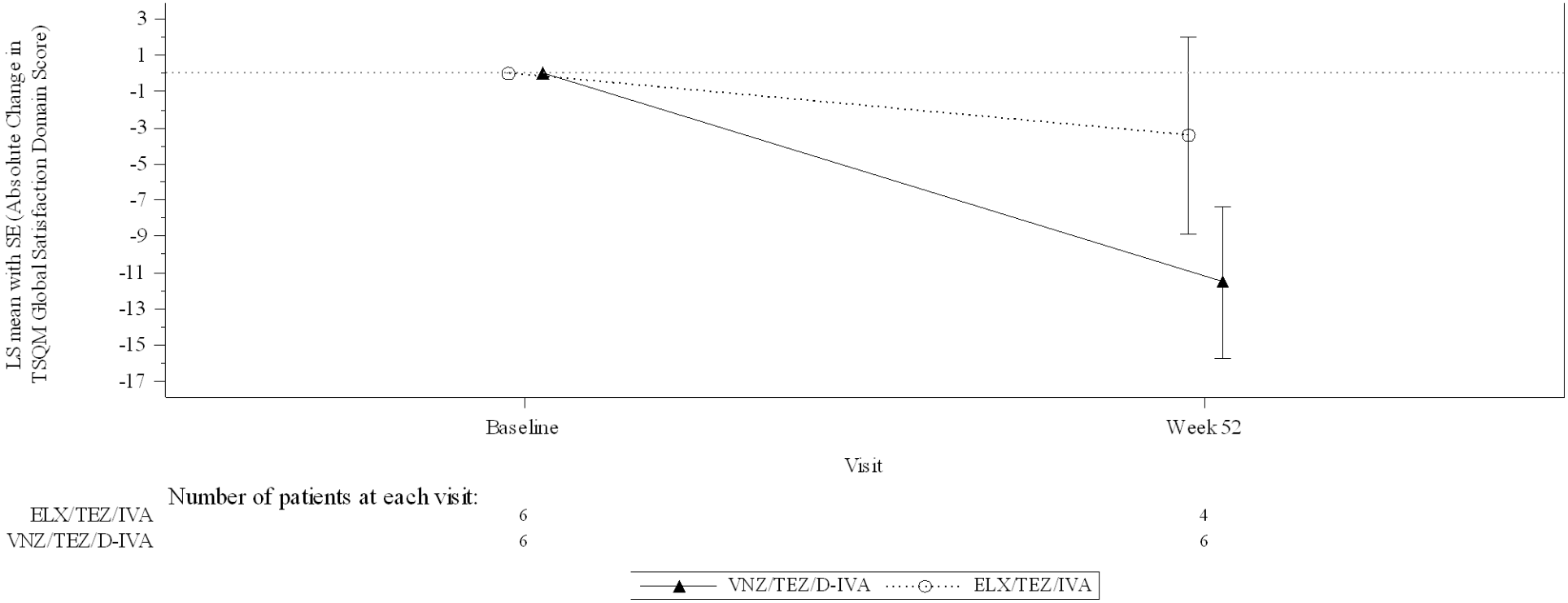
	Baseline	Week 52
ELX/TEZ/IVA	26	23
VNZ/TEZ/D-IVA	24	24

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
ppFEV$_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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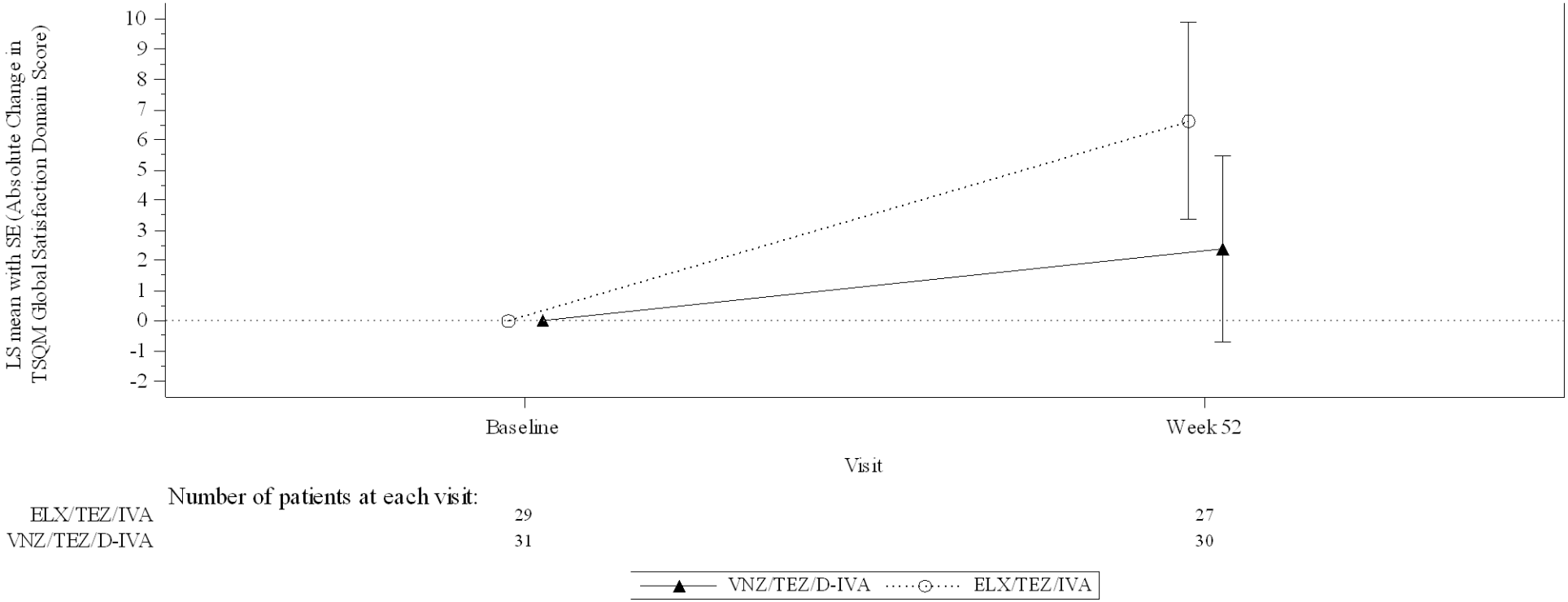
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
ppFEV$_1$ at baseline ≥70 %



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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Age at screening <18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Age at screening ≥18 years

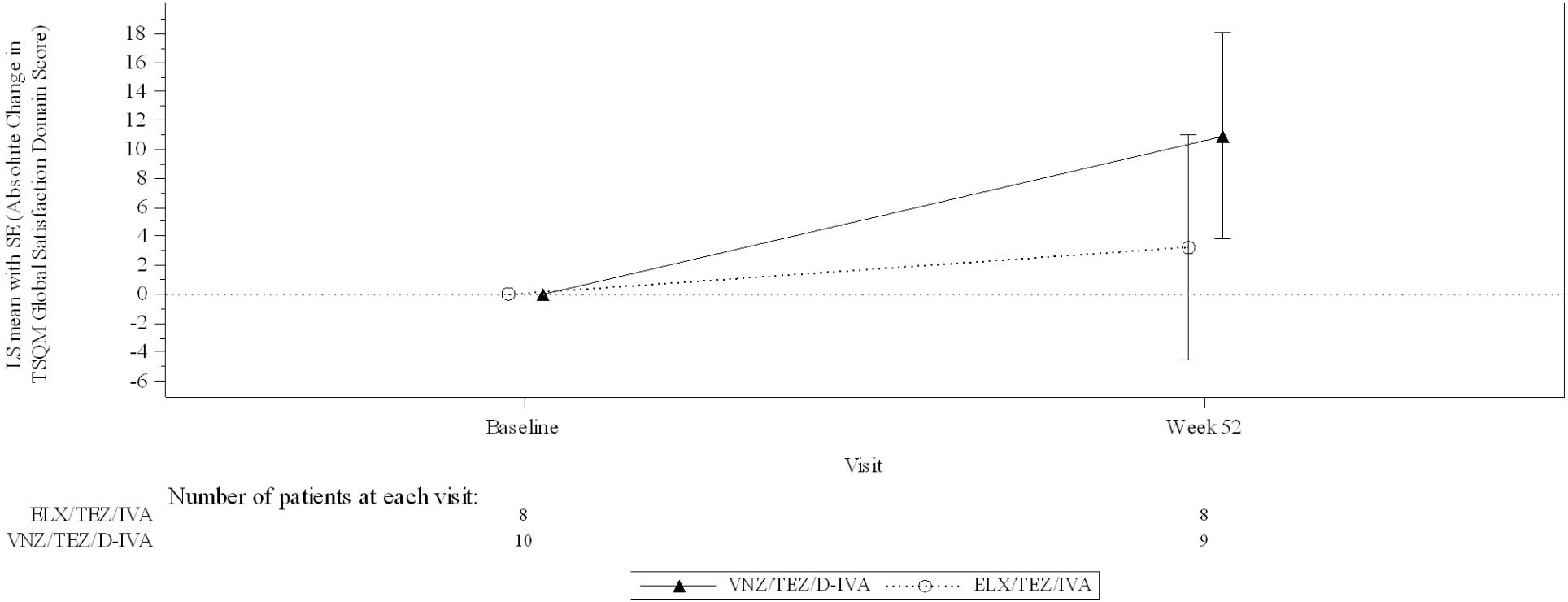
Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
SwCl at baseline <30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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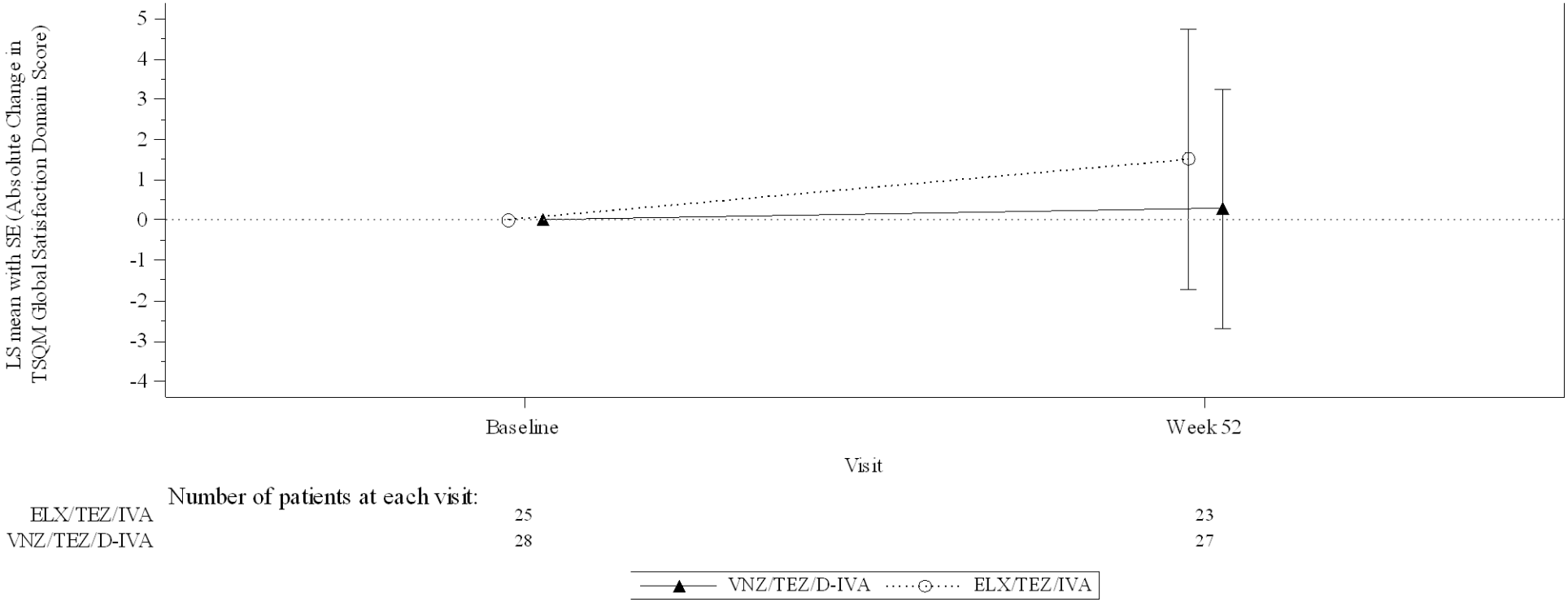
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
SwCl at baseline ≥30 mmol/L



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- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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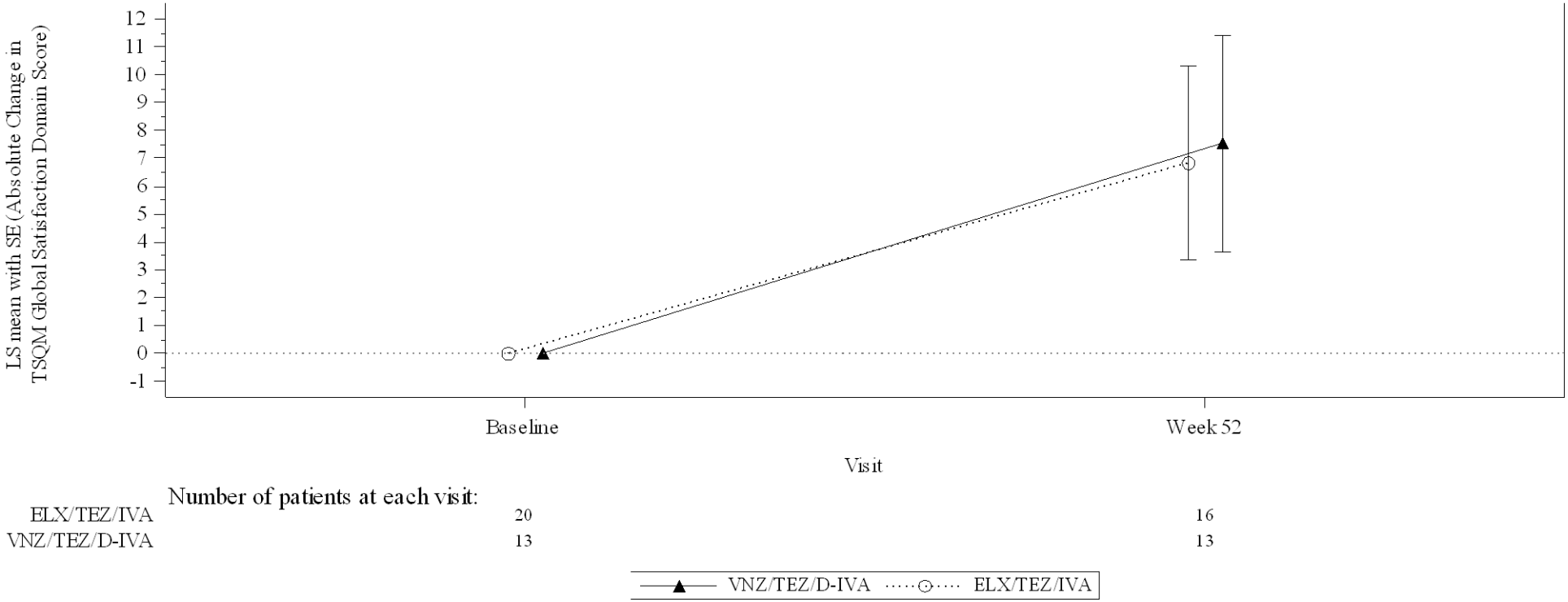
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Male



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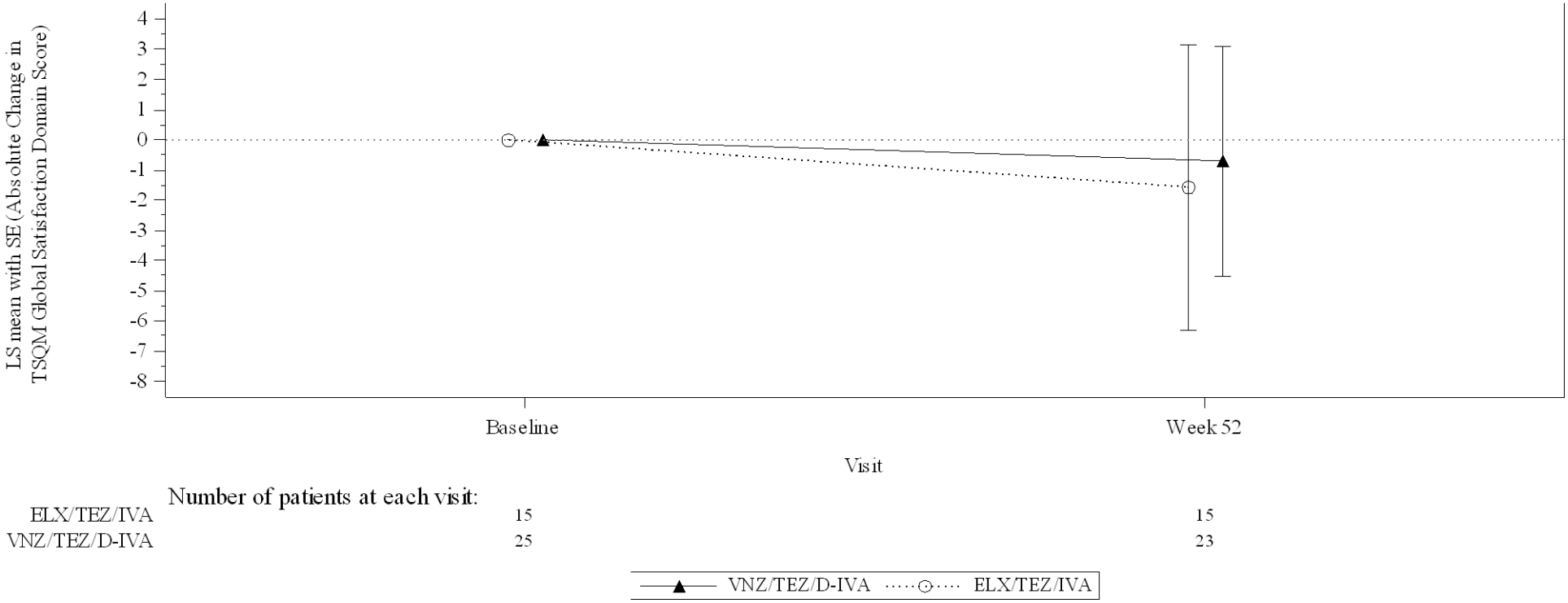
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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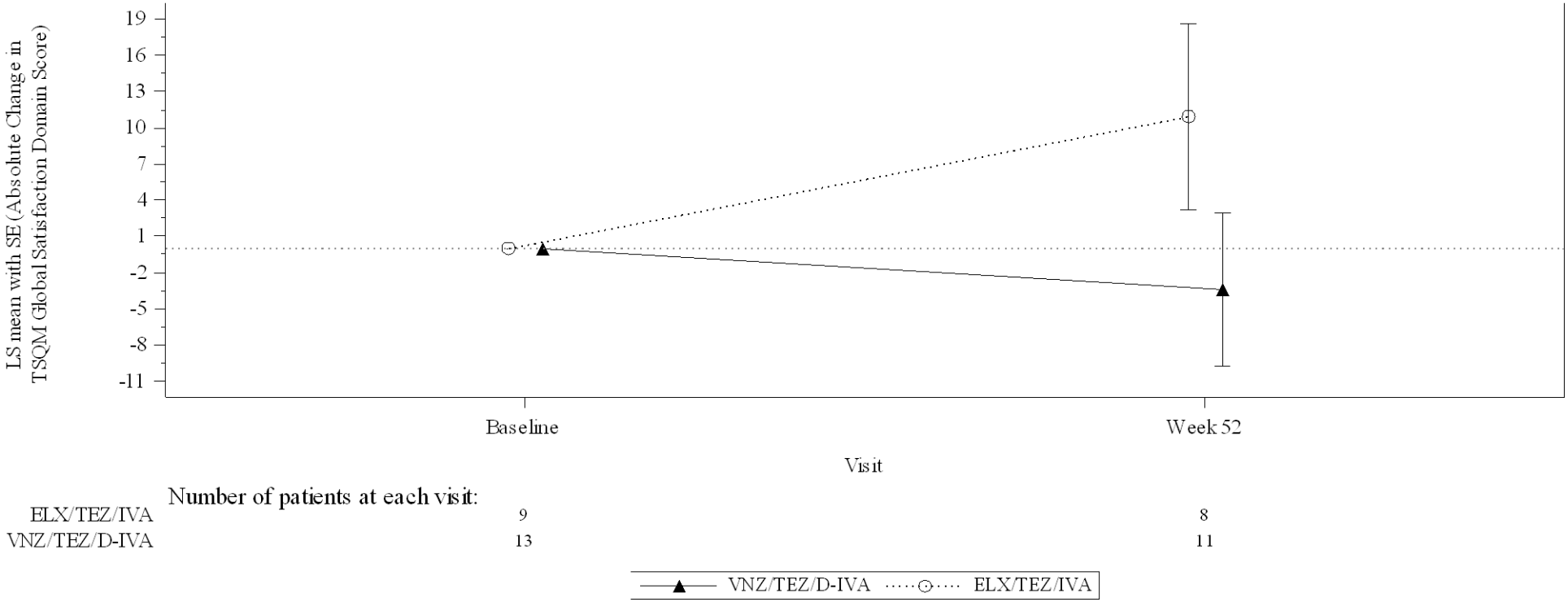
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = North America

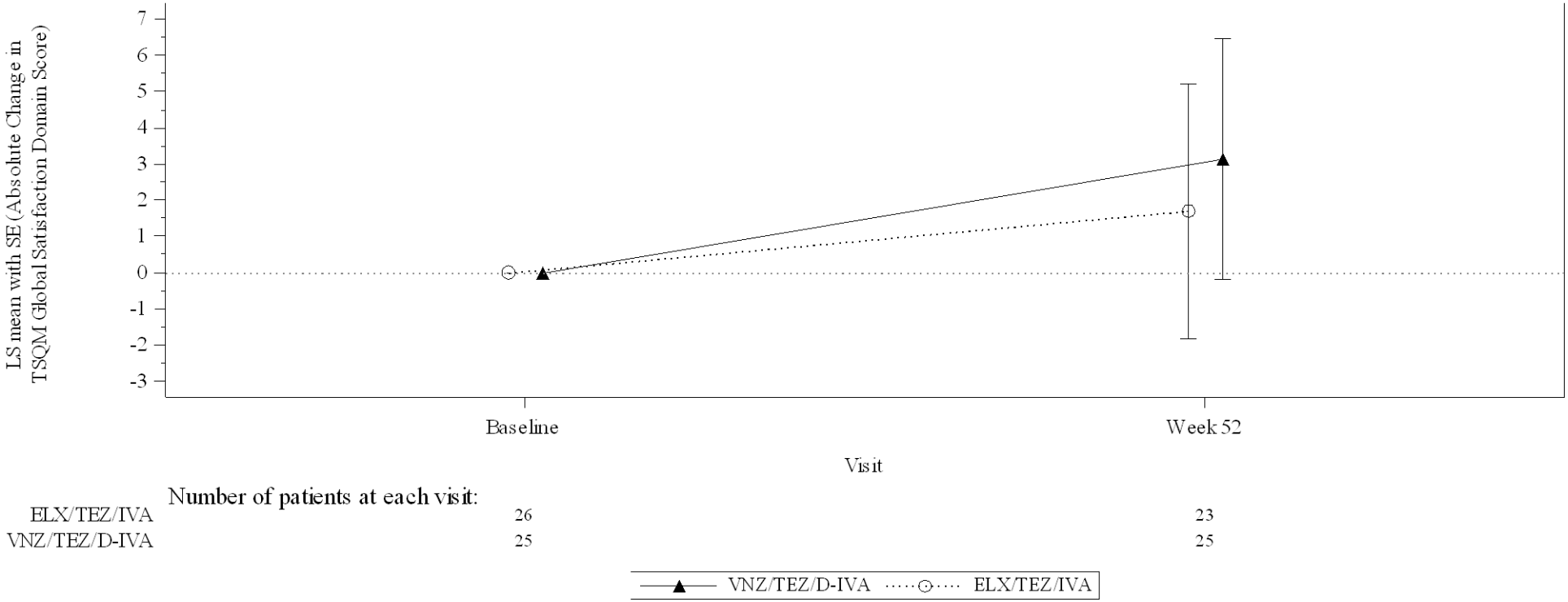


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = Rest of World



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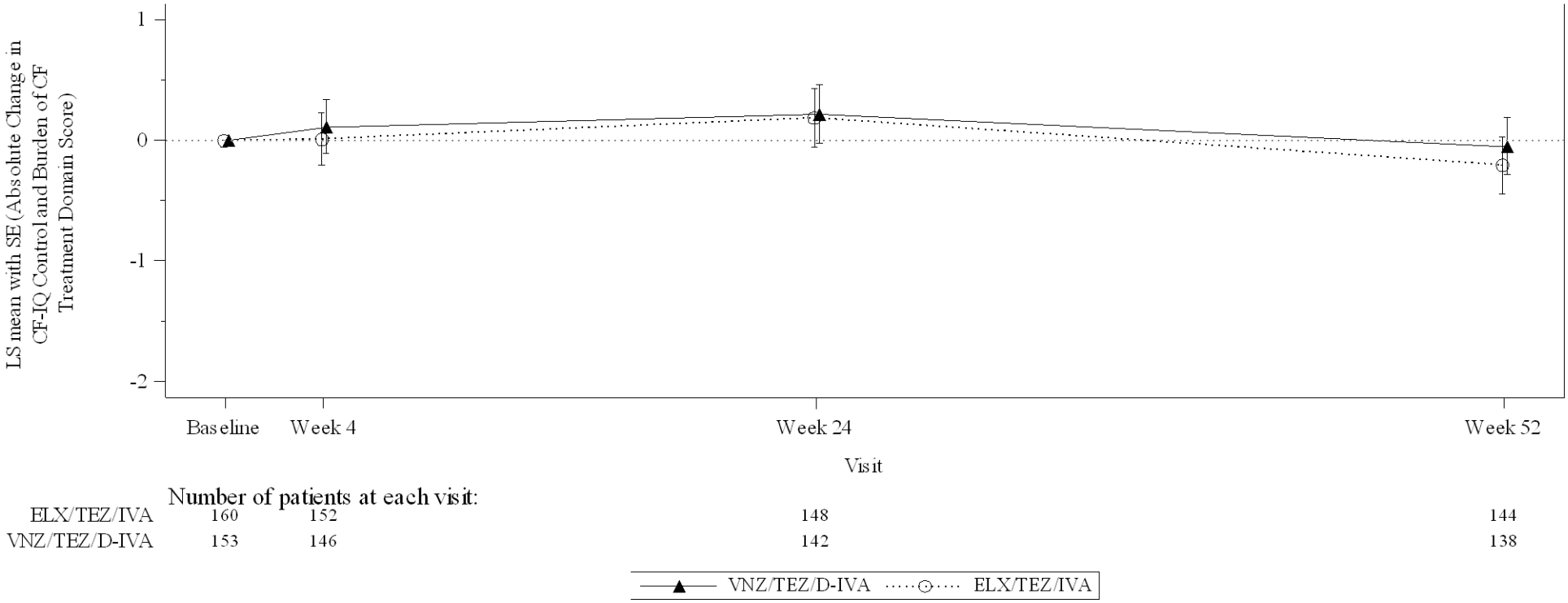
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-tsqm-52wks-sub-103.sas Creation: 07JAN2025 13:48

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
ppFEV$_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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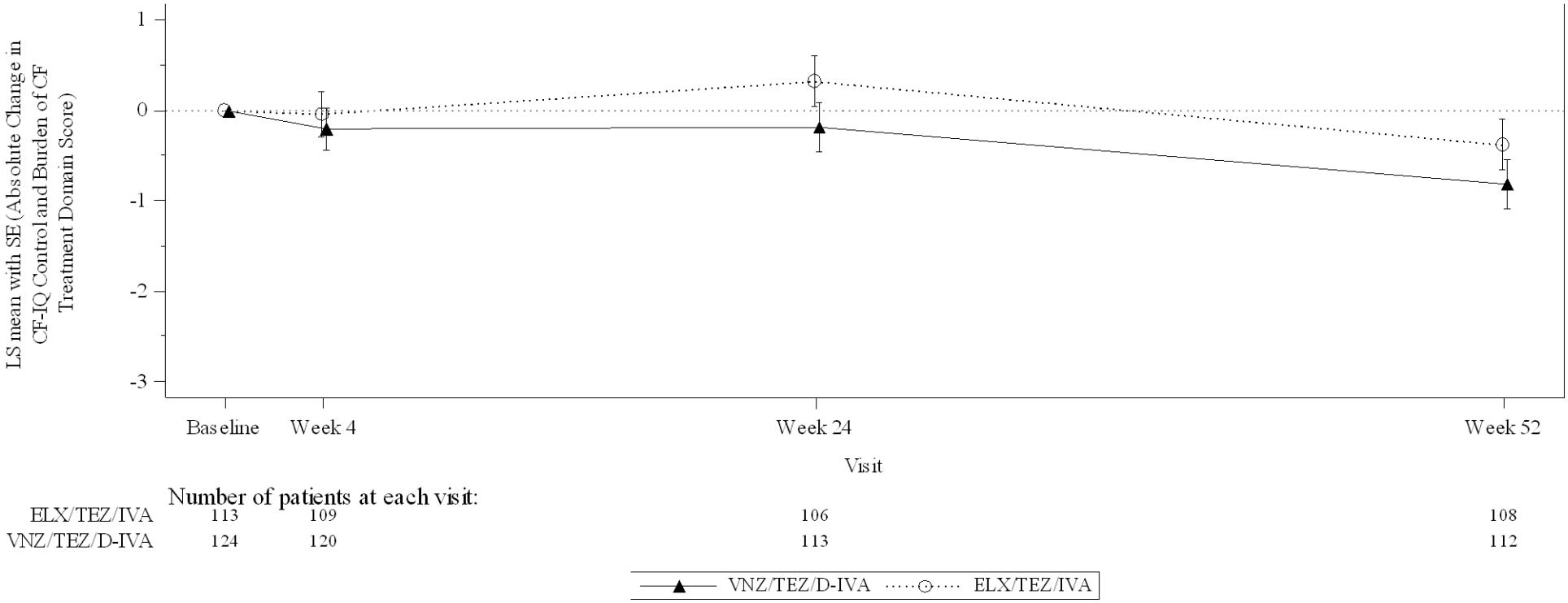
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
ppFEV$_1$ at baseline ≥70 %



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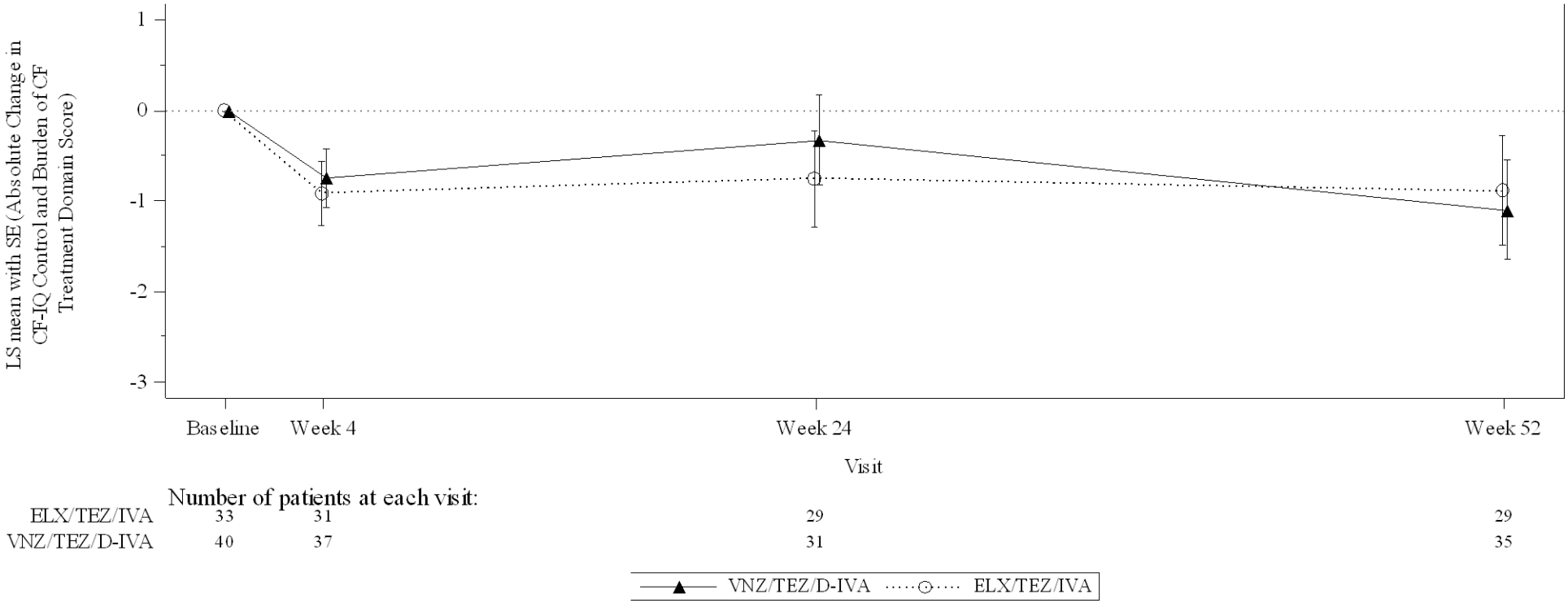
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening <18 years

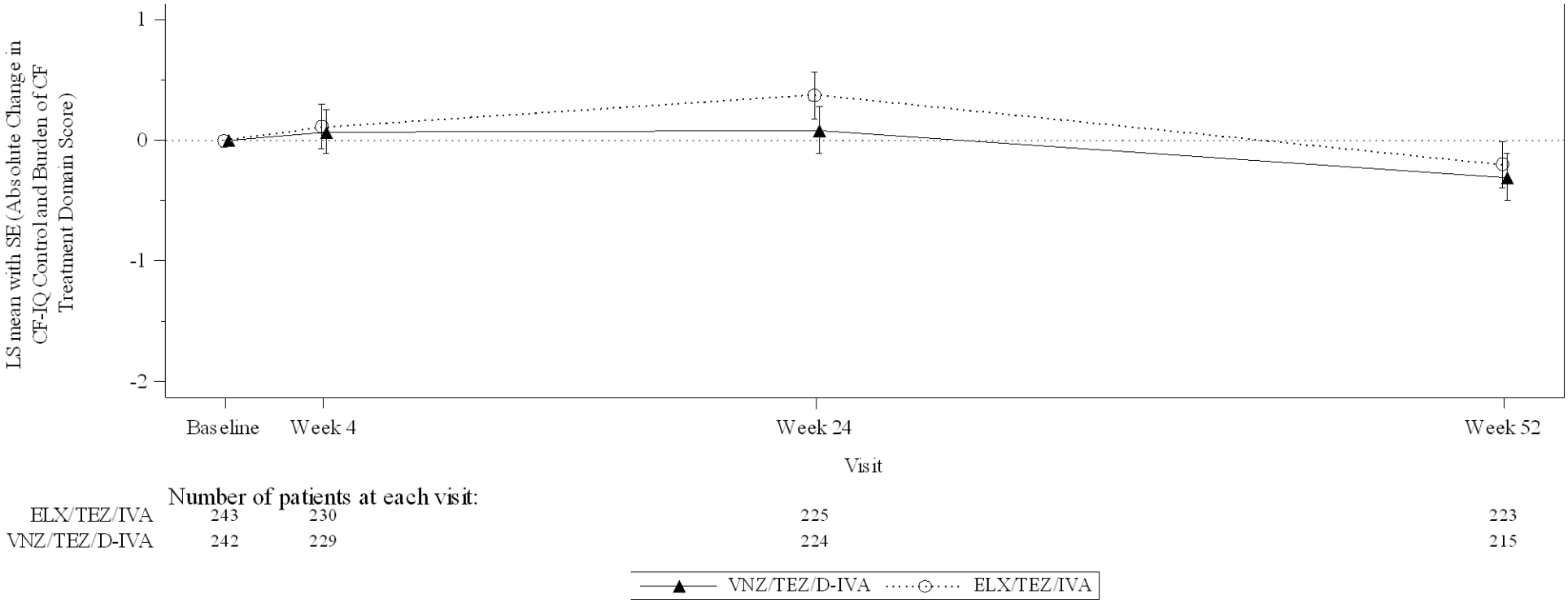


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
Age at screening ≥18 years



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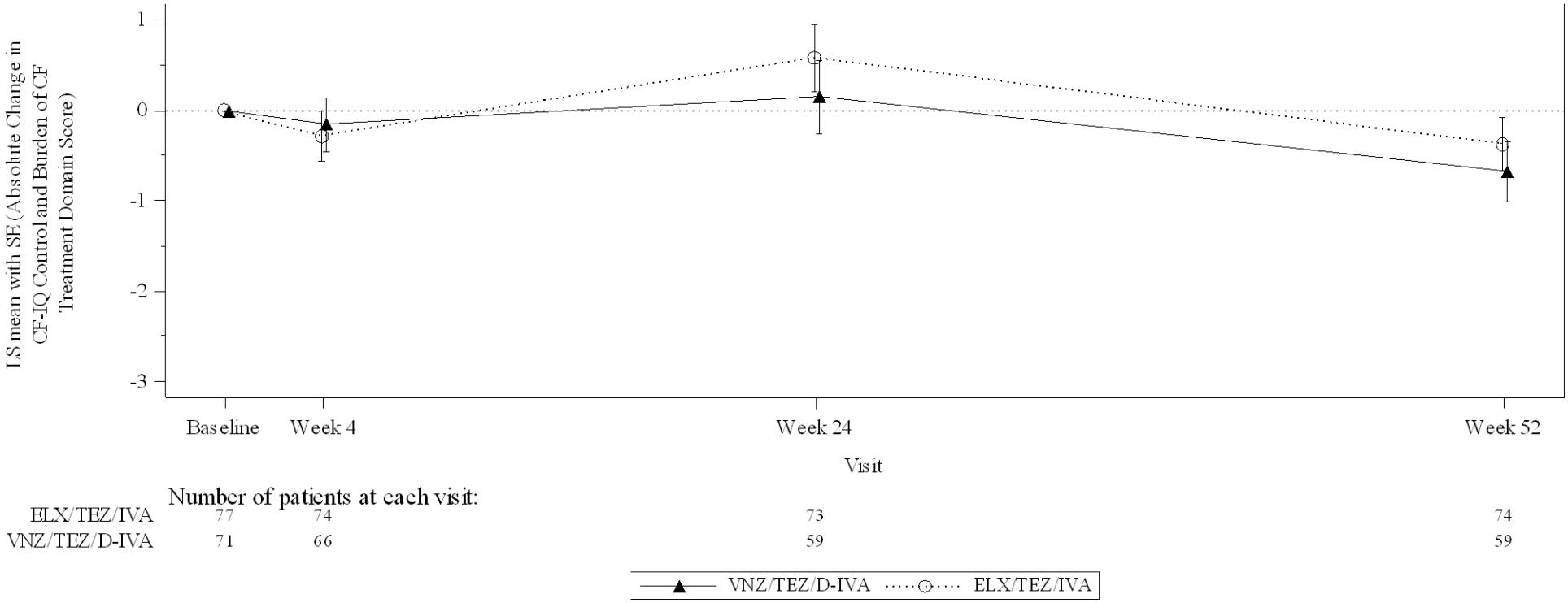
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline <30 mmol/L



Number of patients at each visit:

	Baseline	Week 4	Week 24	Week 52
ELX/TEZ/IVA	77	74	73	74
VNZ/TEZ/D-IVA	71	66	59	59

VNZ/TEZ/D-IVA ELX/TEZ/IVA

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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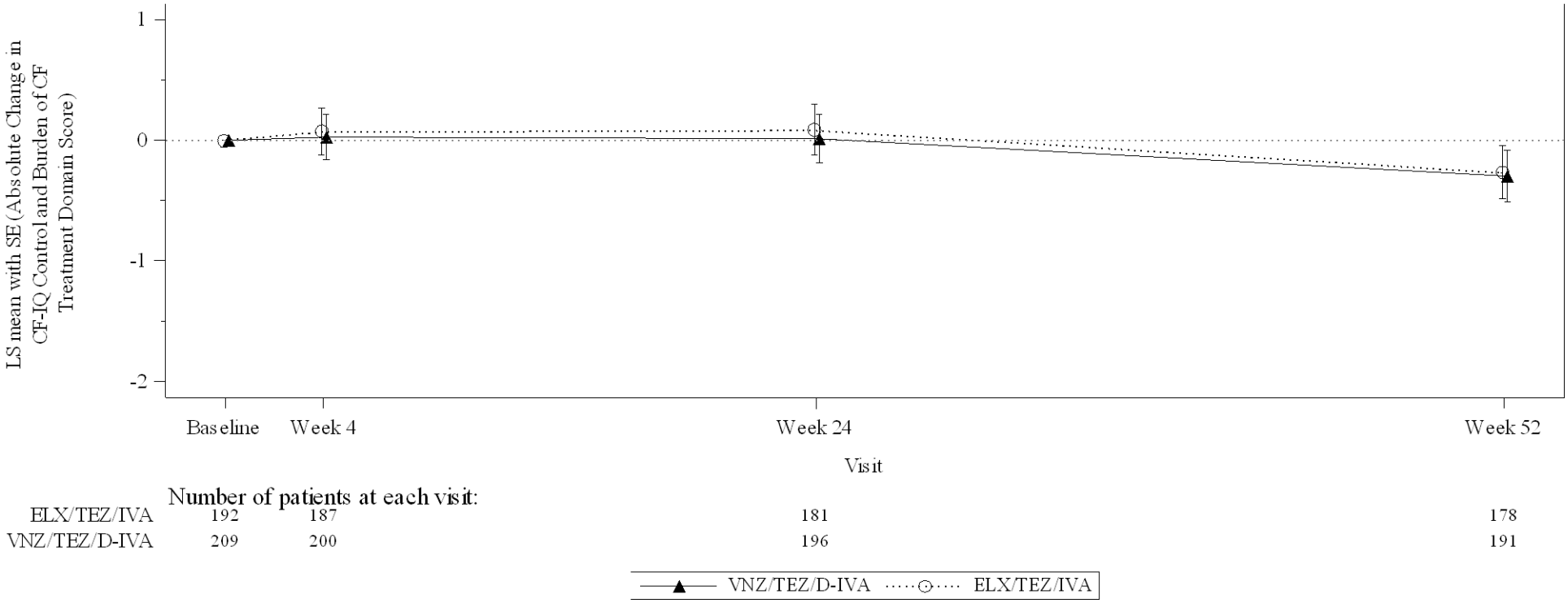
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
SwCl at baseline ≥30 mmol/L



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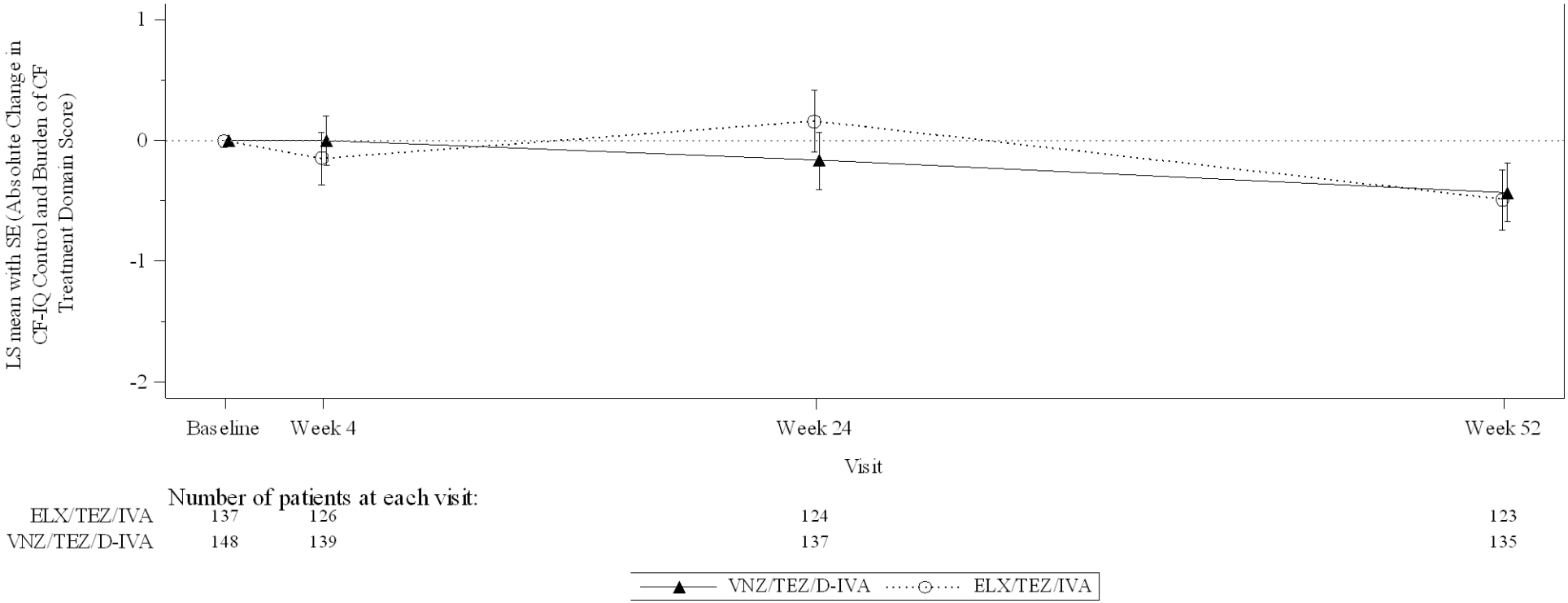
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Male



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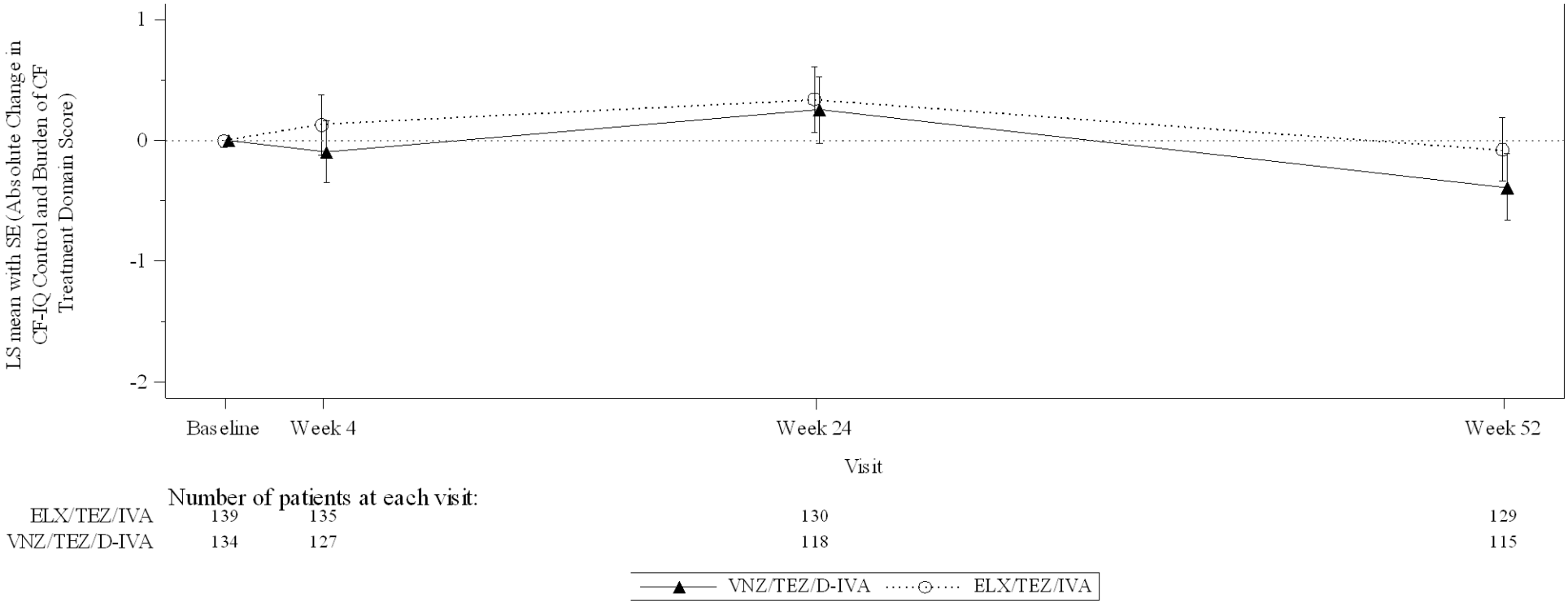
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
Sex = Female



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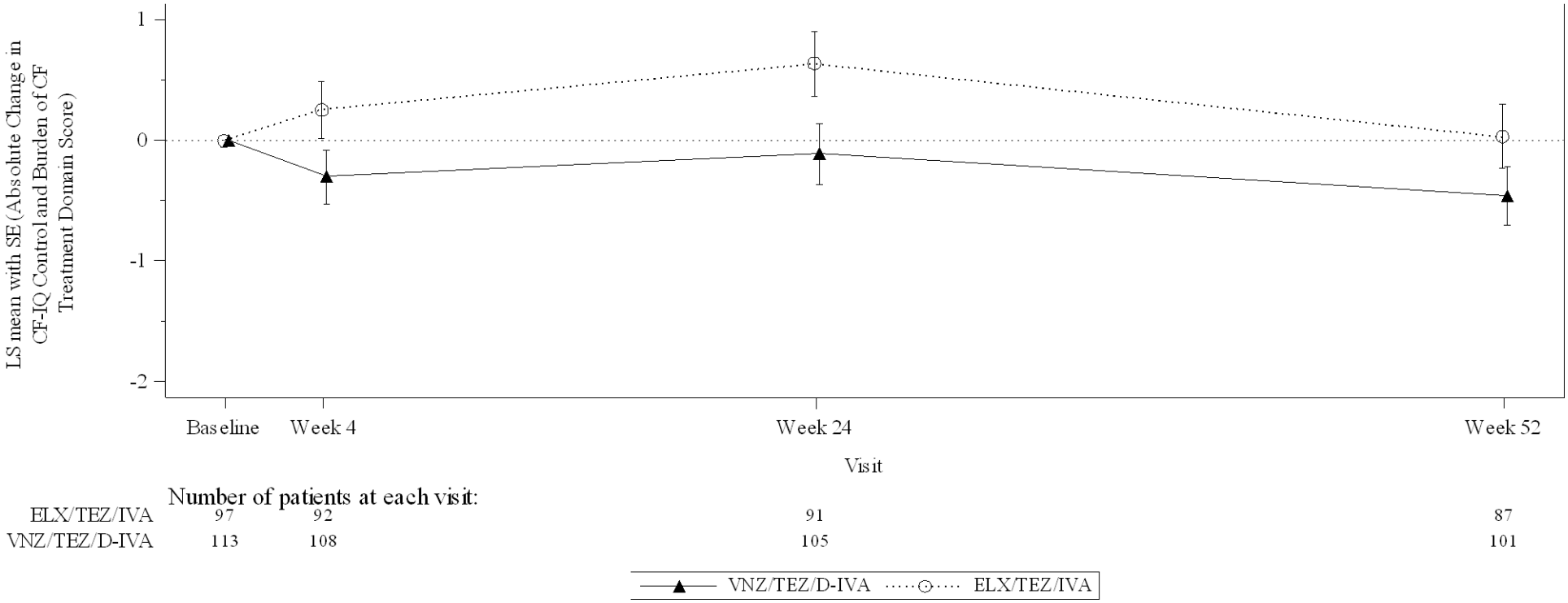
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = North America



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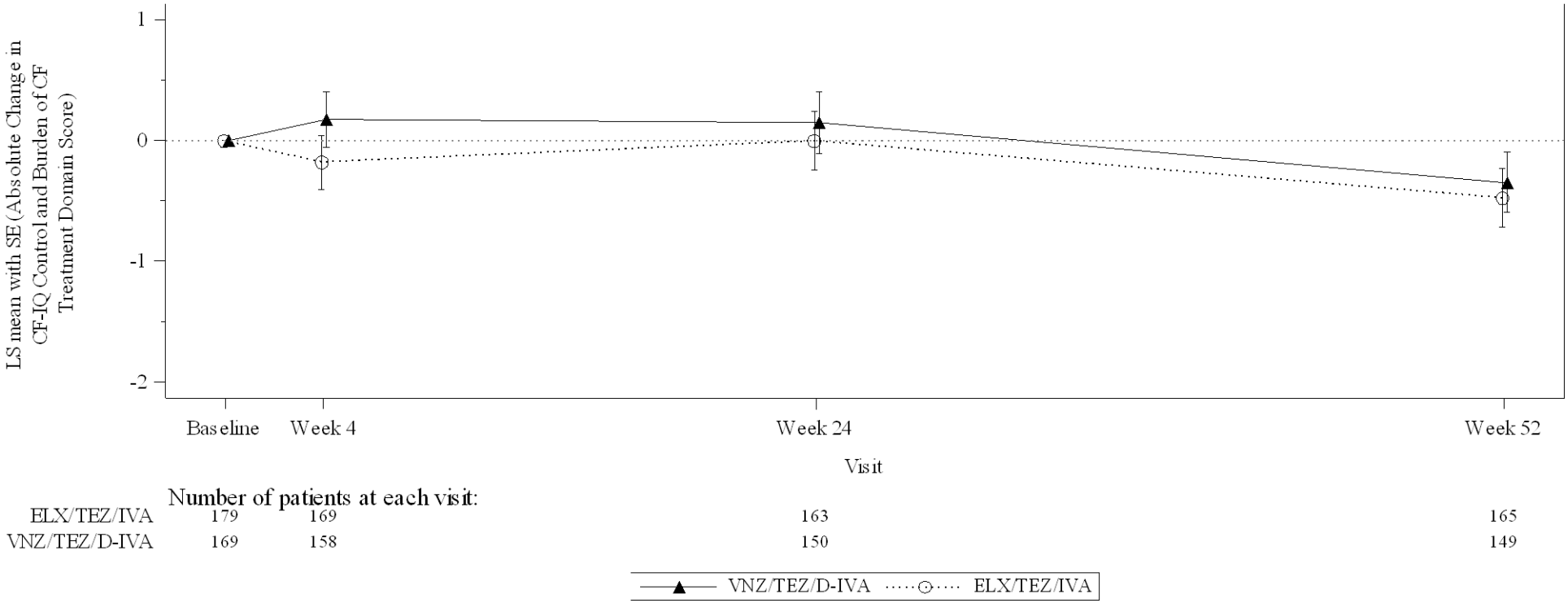
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Control and Burden of CF Treatment
Region = Rest of World



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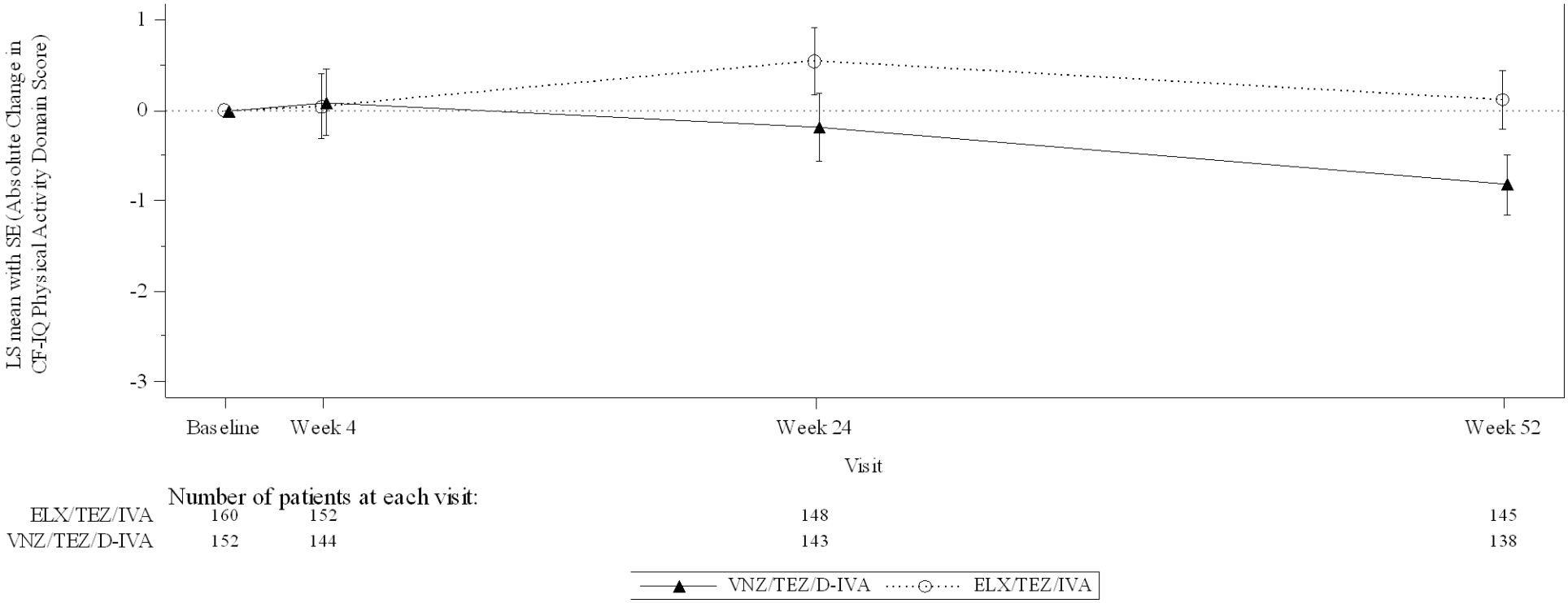
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
ppFEV$_1$ at baseline <70 %

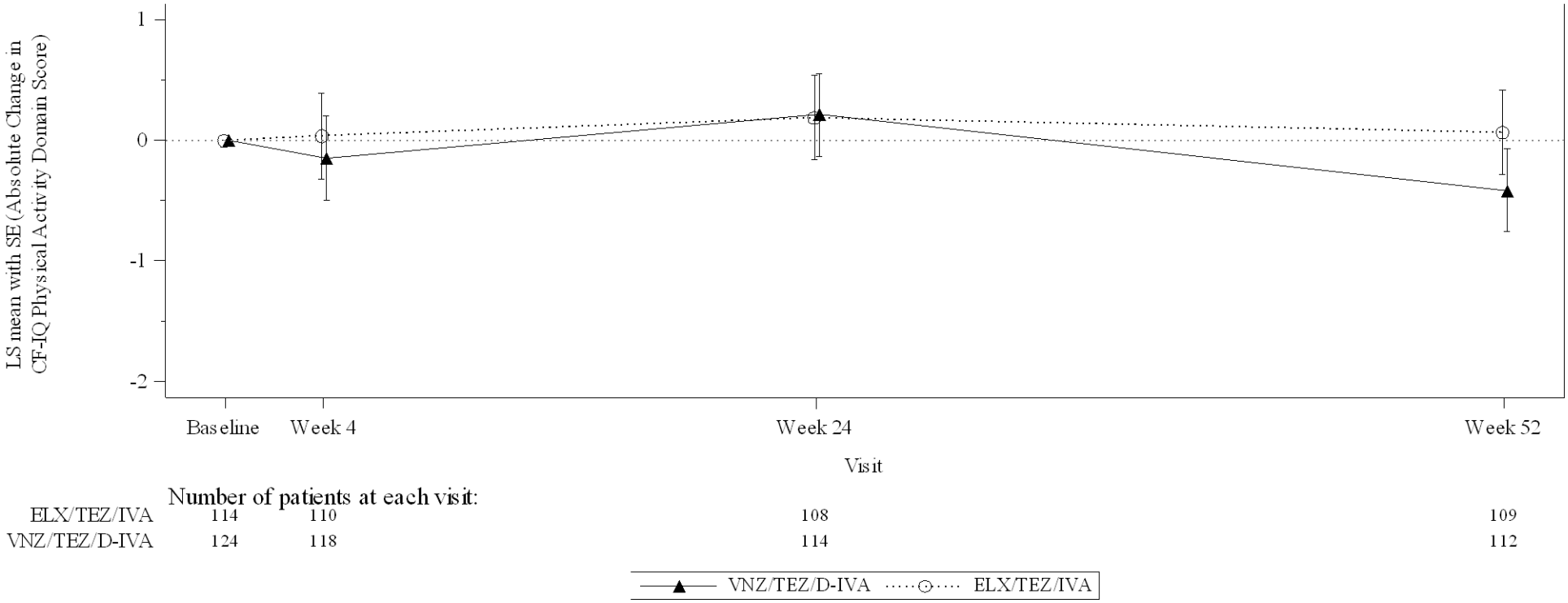


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
ppFEV$_1$ at baseline ≥70 %

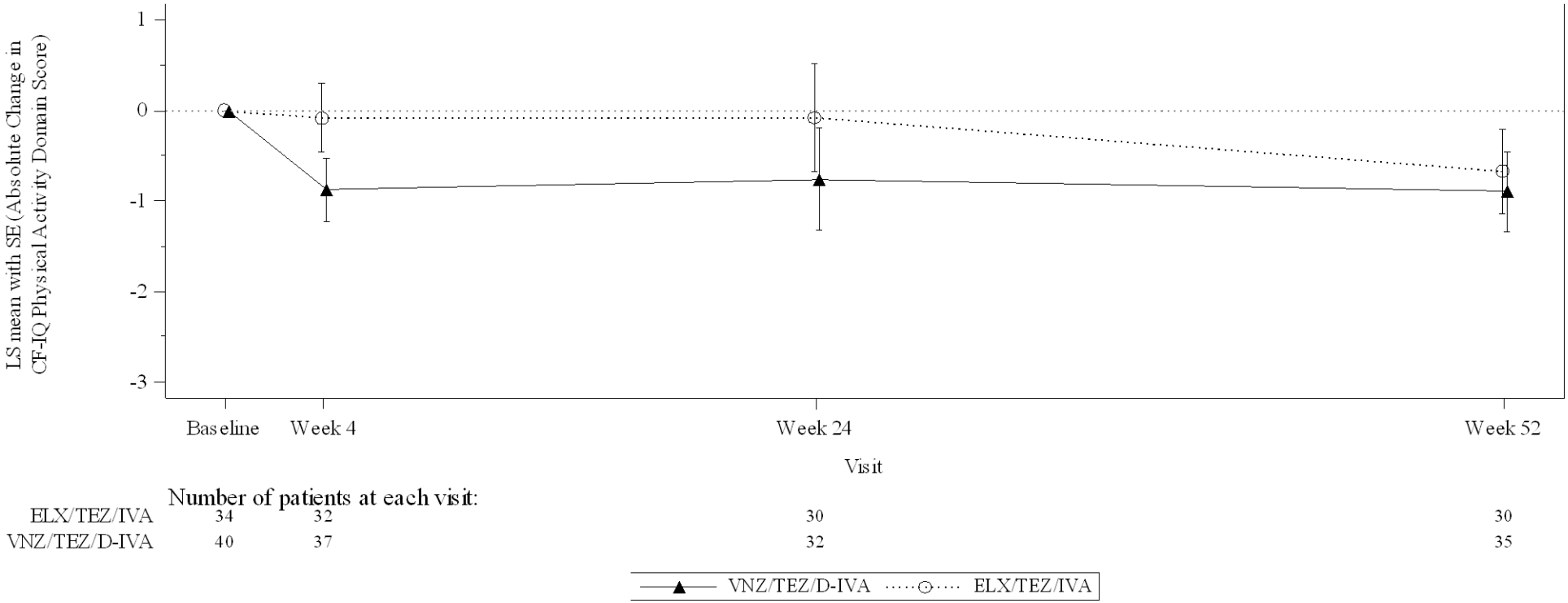


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
Age at screening <18 years

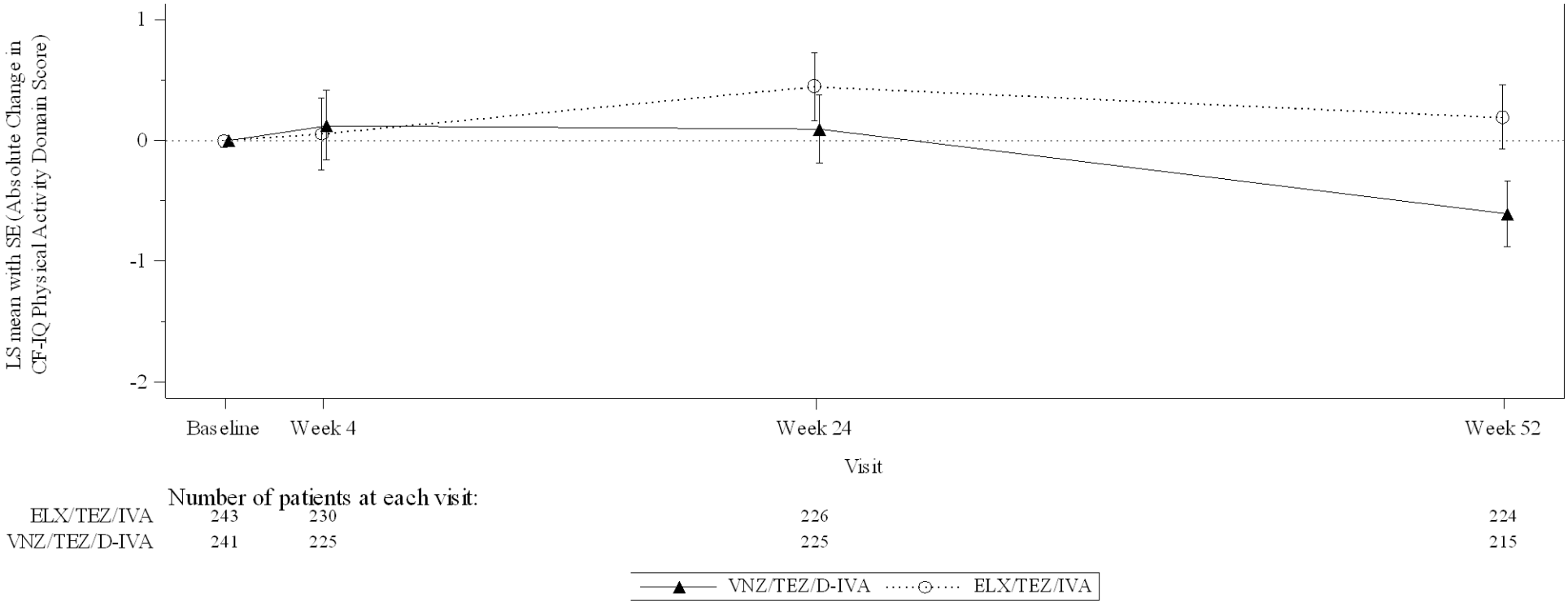


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
Age at screening ≥18 years



Number of patients at each visit:

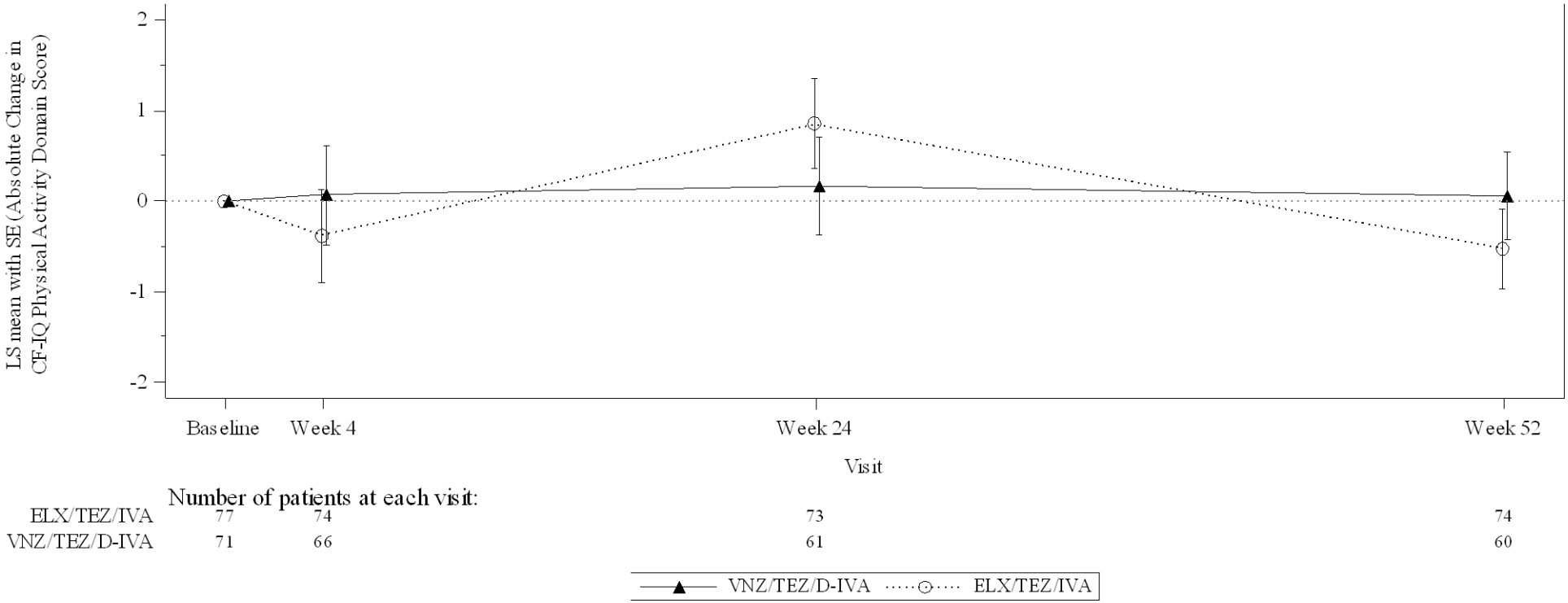
	Baseline	Week 4	Week 24	Week 52
ELX/TEZ/IVA	243	230	226	224
VNZ/TEZ/D-IVA	241	225	225	215

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
SwCl at baseline <30 mmol/L

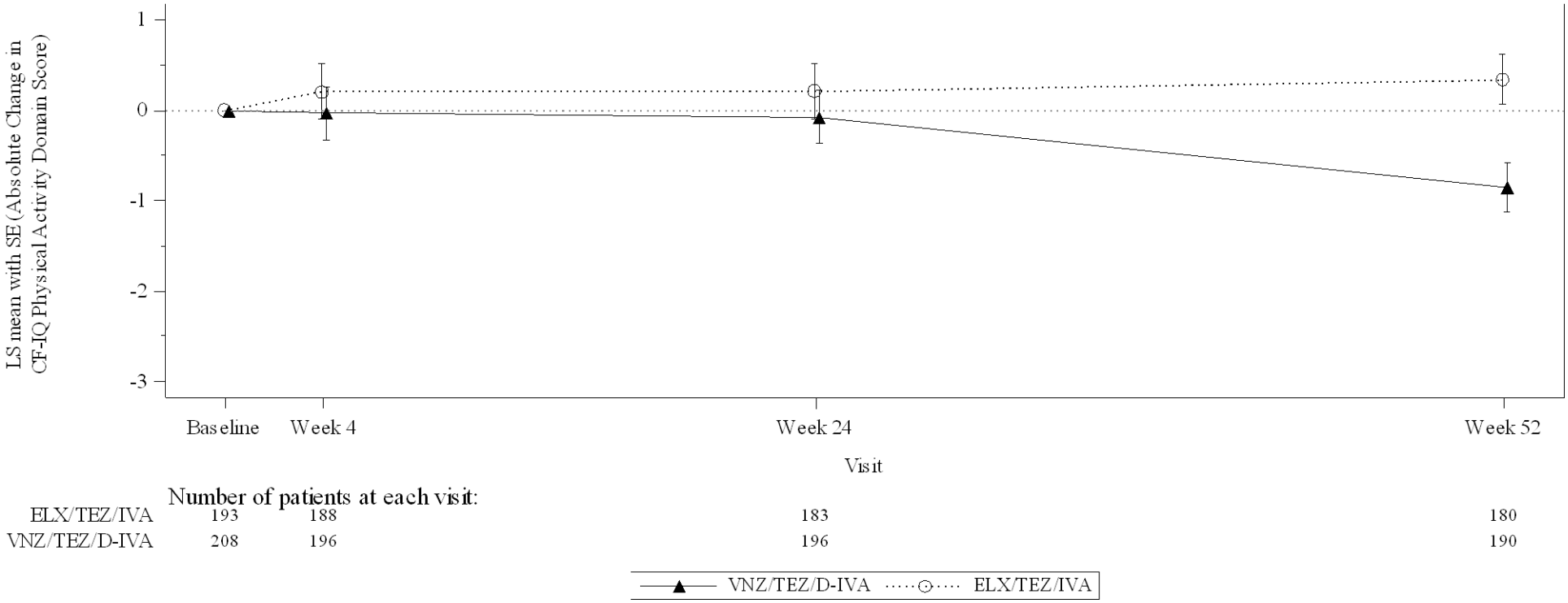


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
SwCl at baseline ≥30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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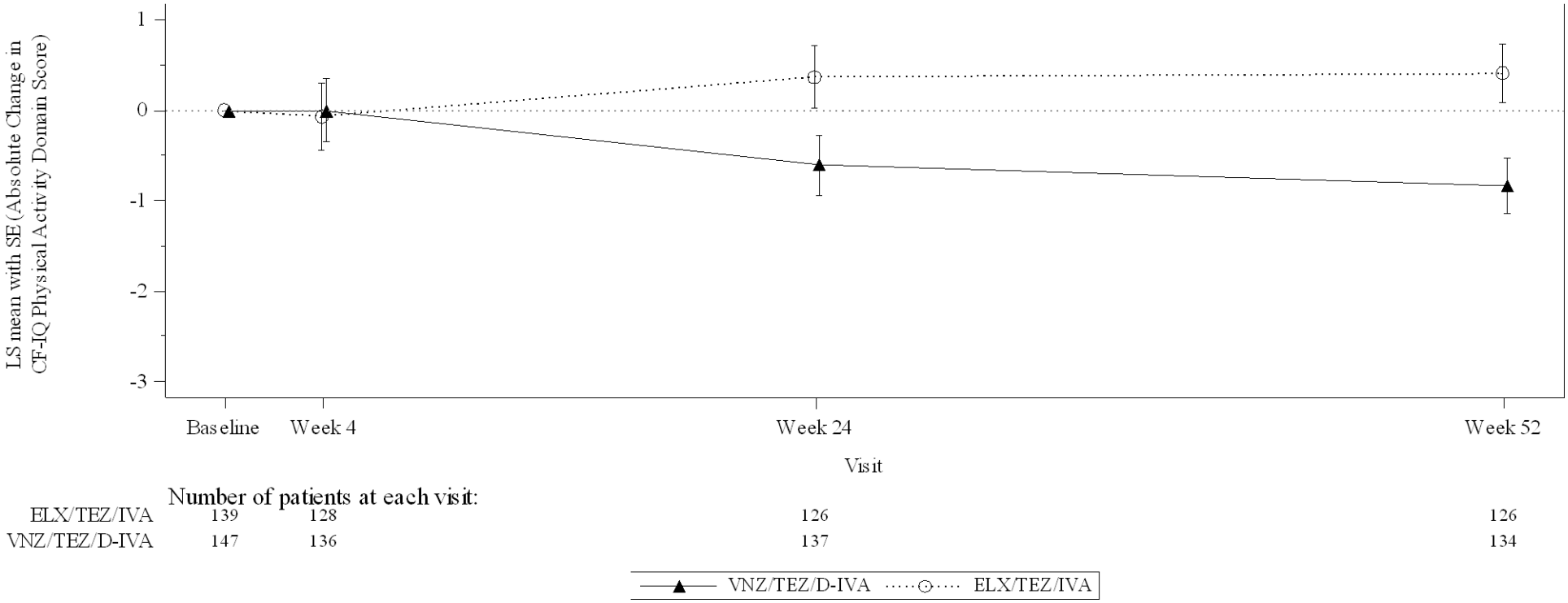
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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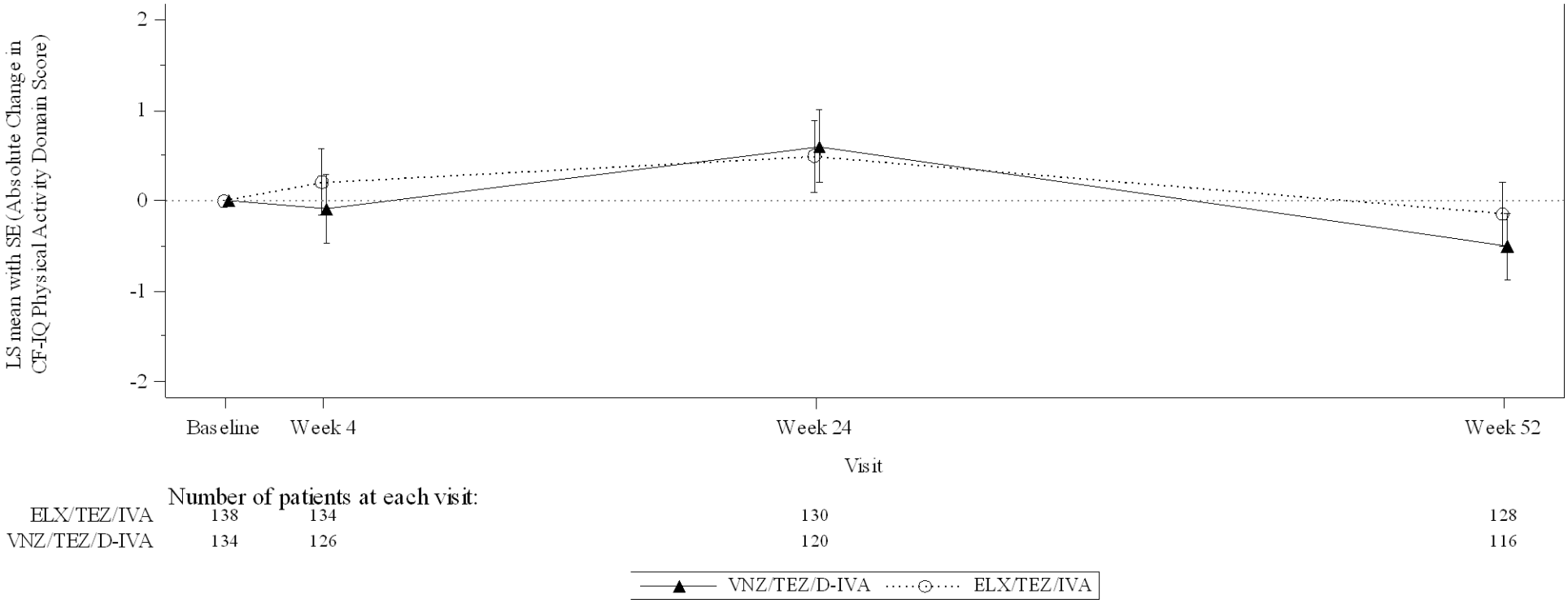
Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
Sex = Female

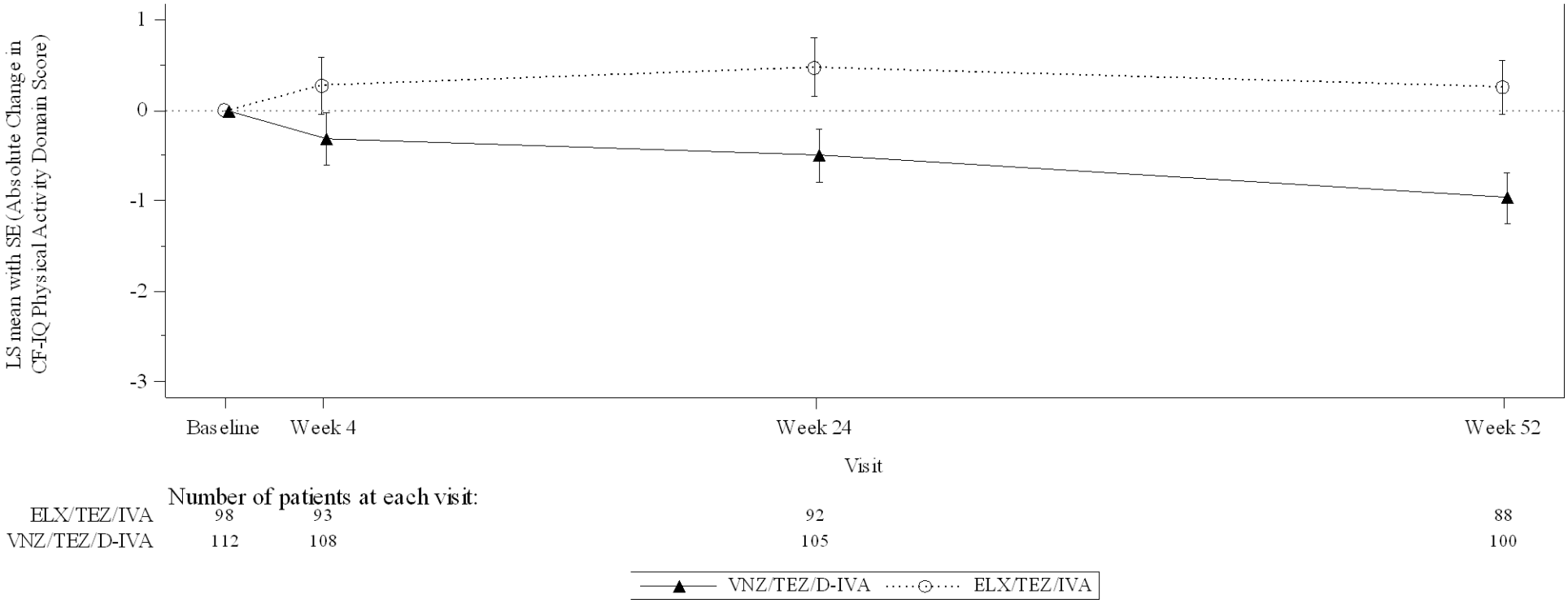


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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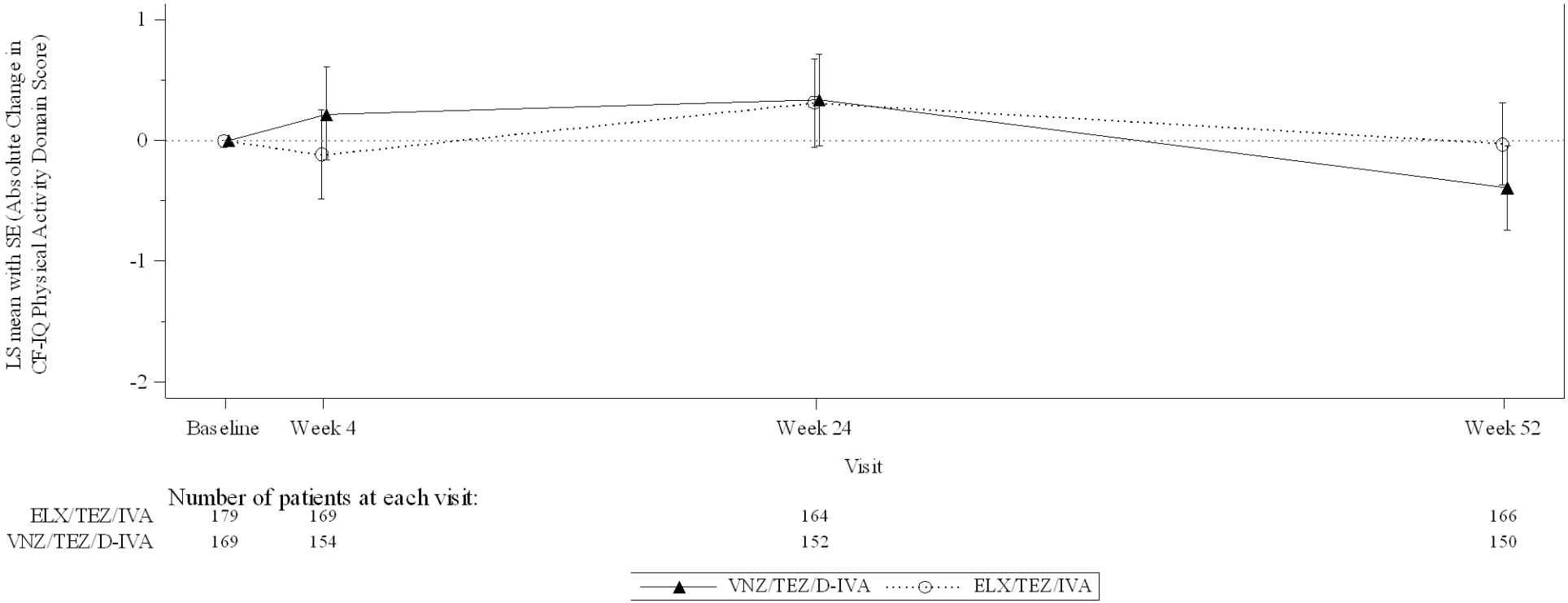
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Physical Activity
Region = Rest of World



Number of patients at each visit:

	Baseline	Week 4	Week 24	Week 52
ELX/TEZ/IVA	179	169	164	166
VNZ/TEZ/D-IVA	169	154	152	150

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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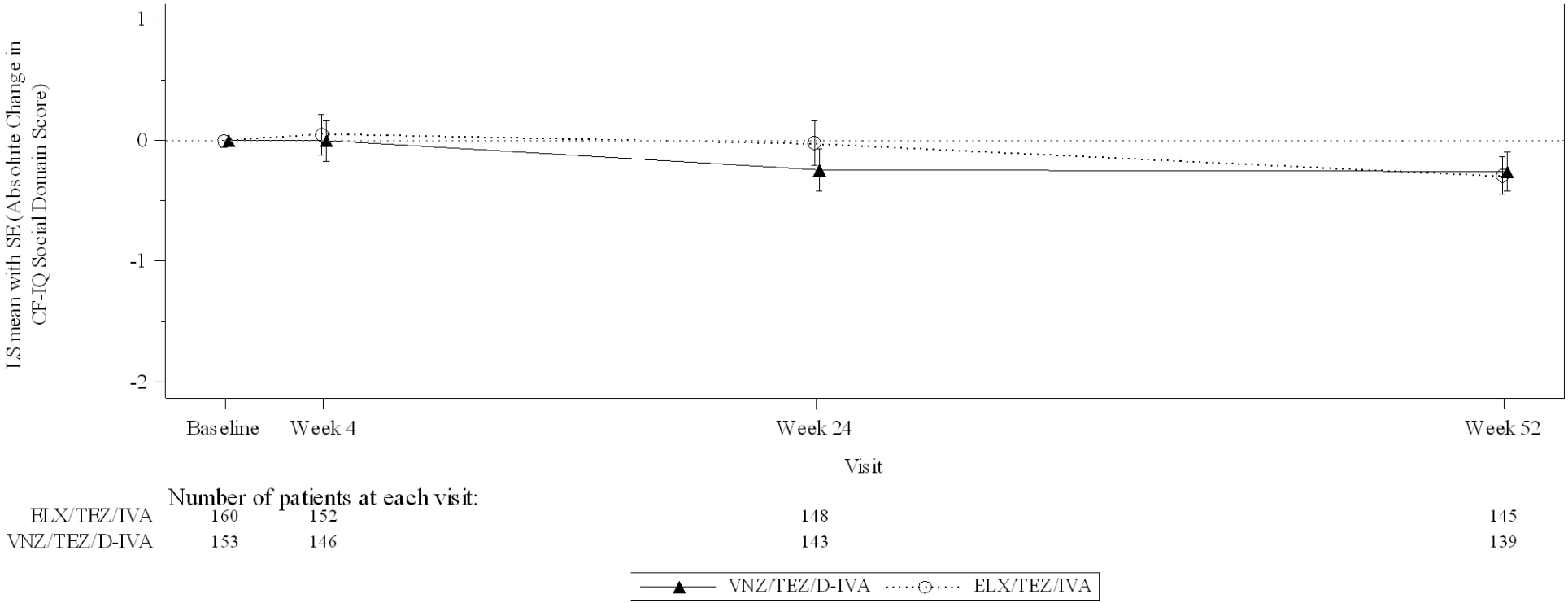
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
ppFEV$_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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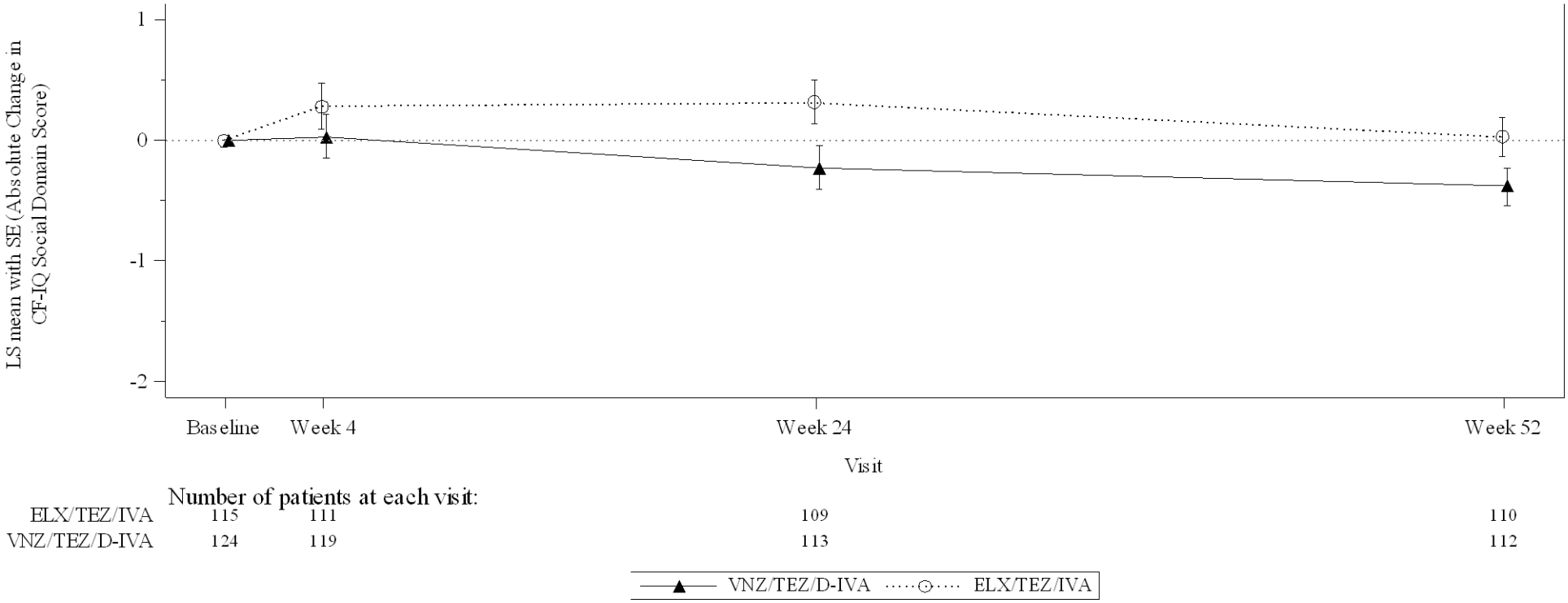
Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
ppFEV$_1$ at baseline ≥70 %



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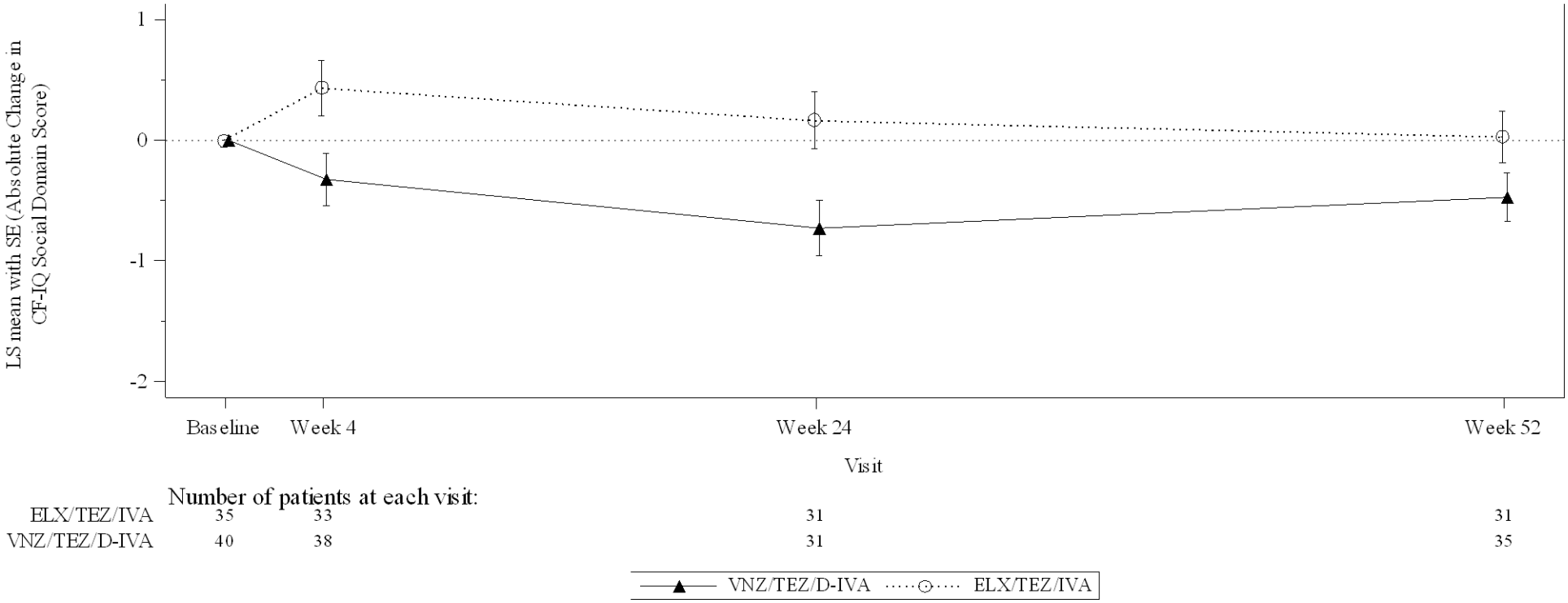
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
Age at screening <18 years



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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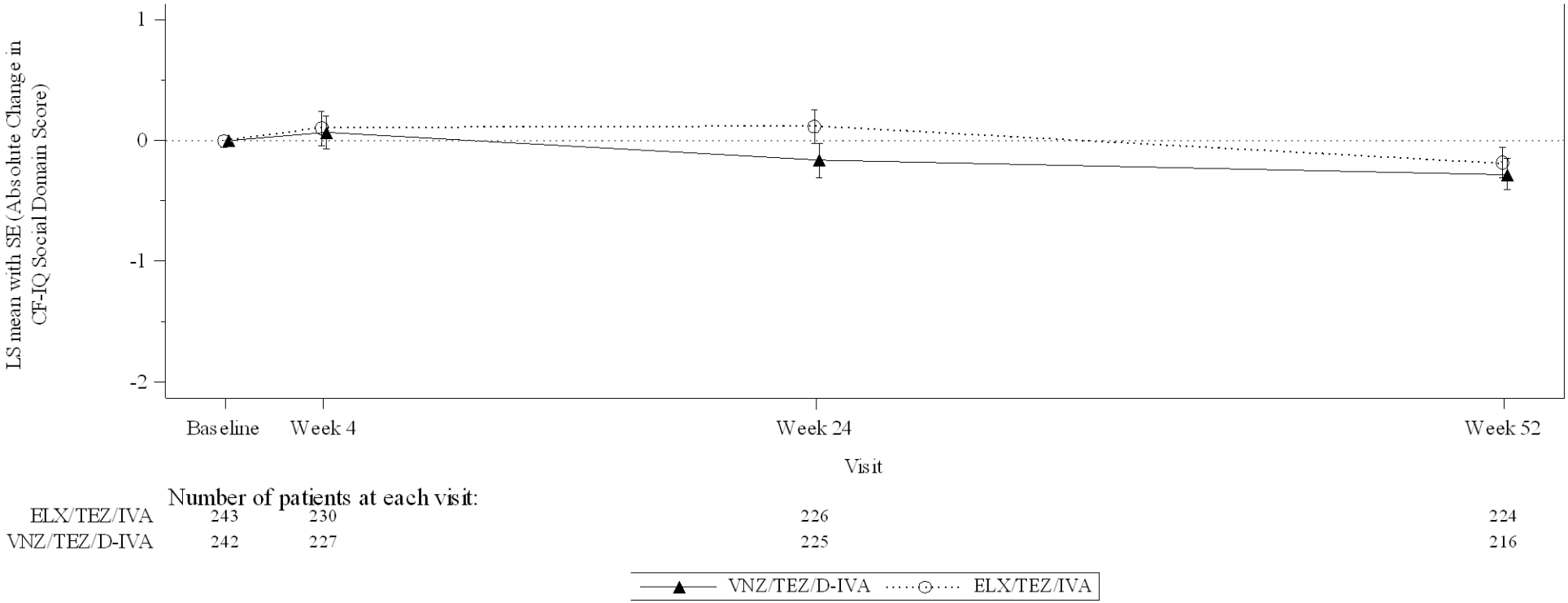
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
Age at screening ≥18 years



Number of patients at each visit:

	Baseline	Week 4	Week 24	Week 52
ELX/TEZ/IVA	243	230	226	224
VNZ/TEZ/D-IVA	242	227	225	216

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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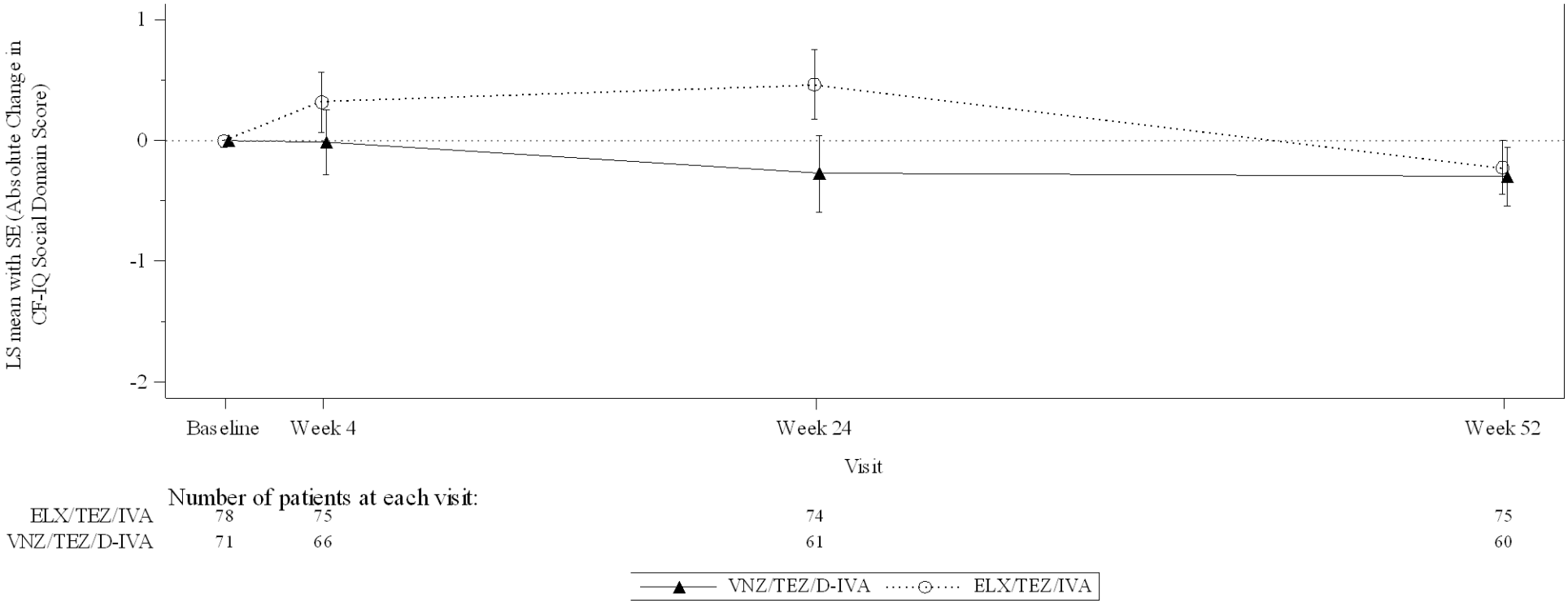
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
SwCl at baseline <30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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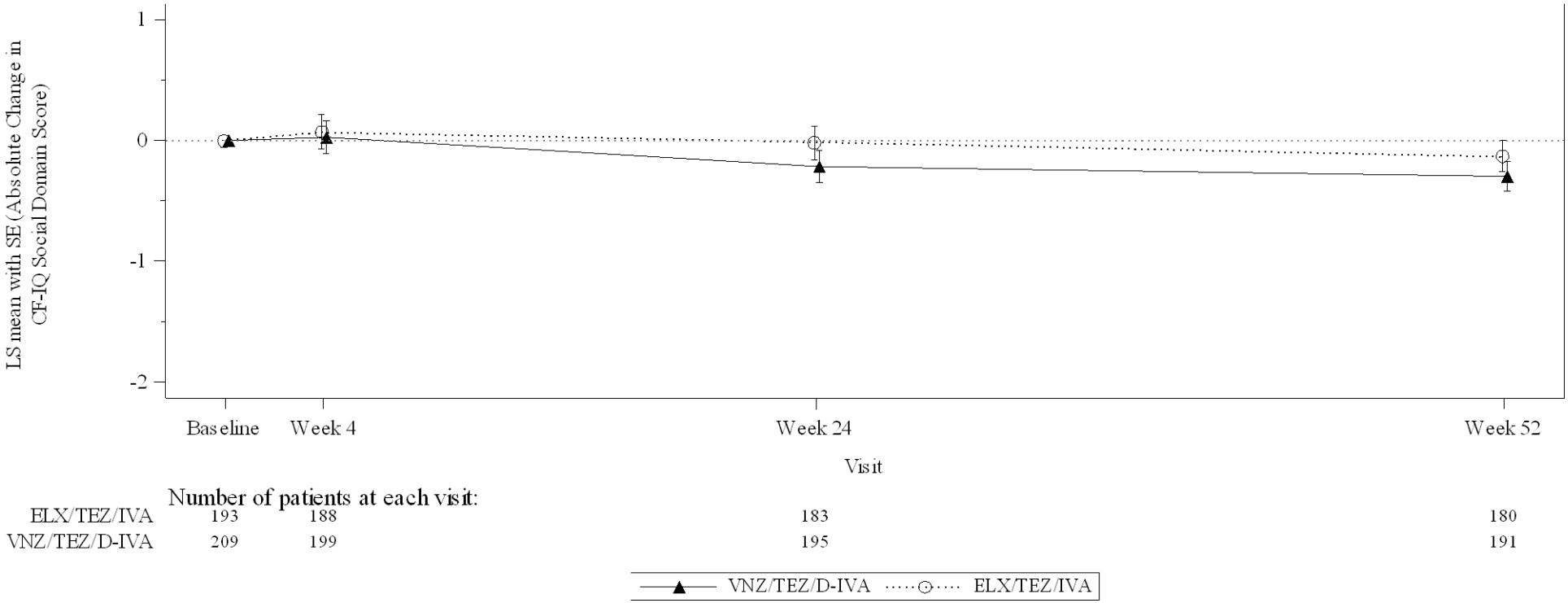
Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
SwCl at baseline ≥30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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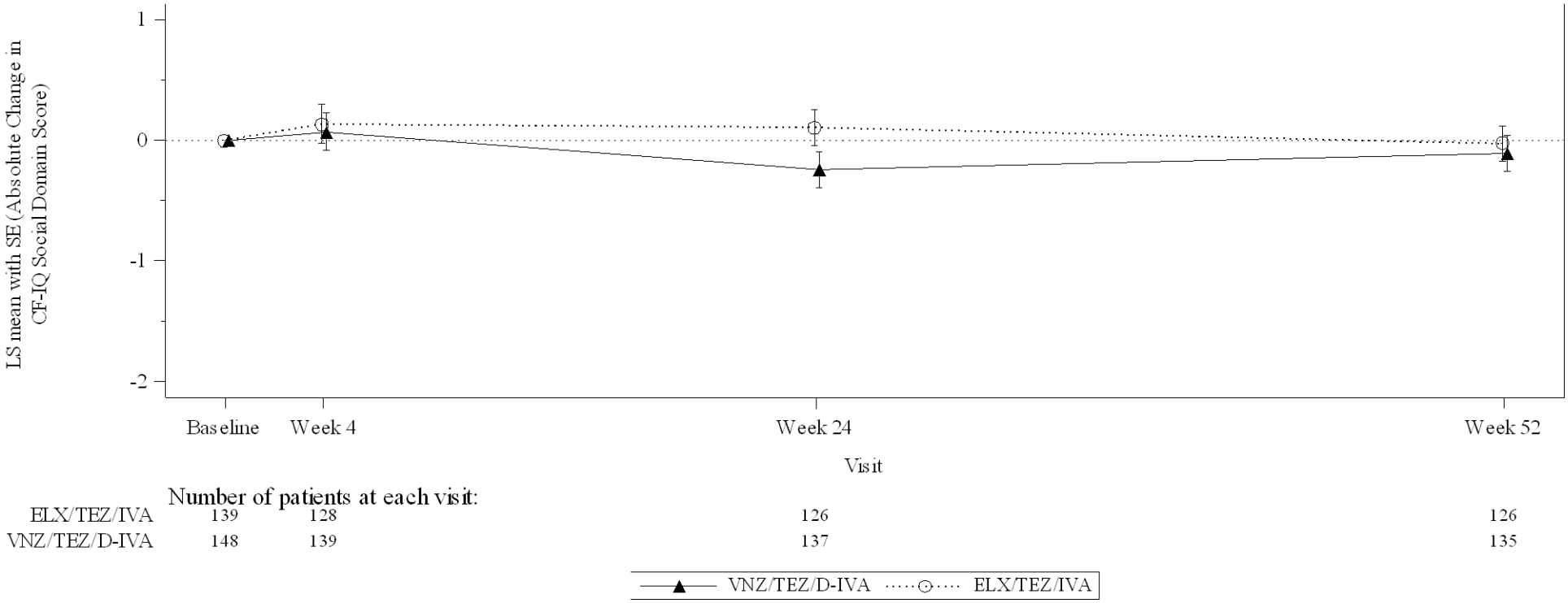
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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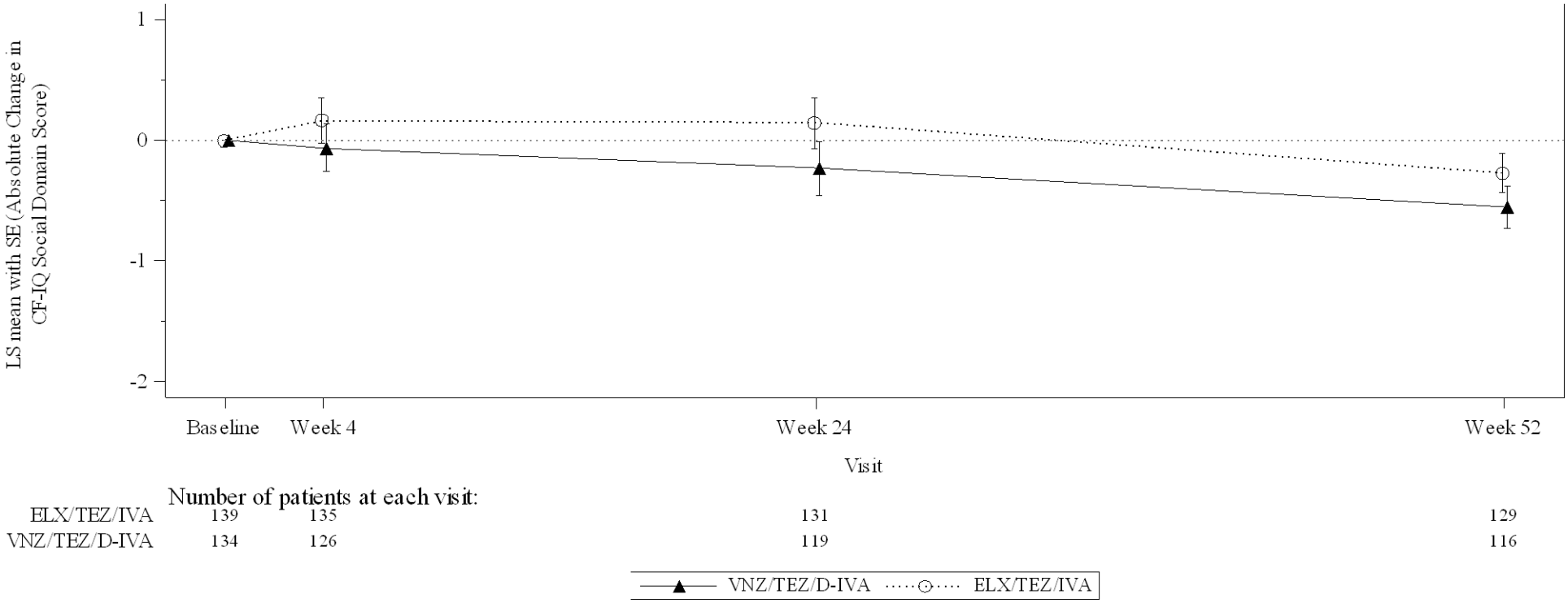
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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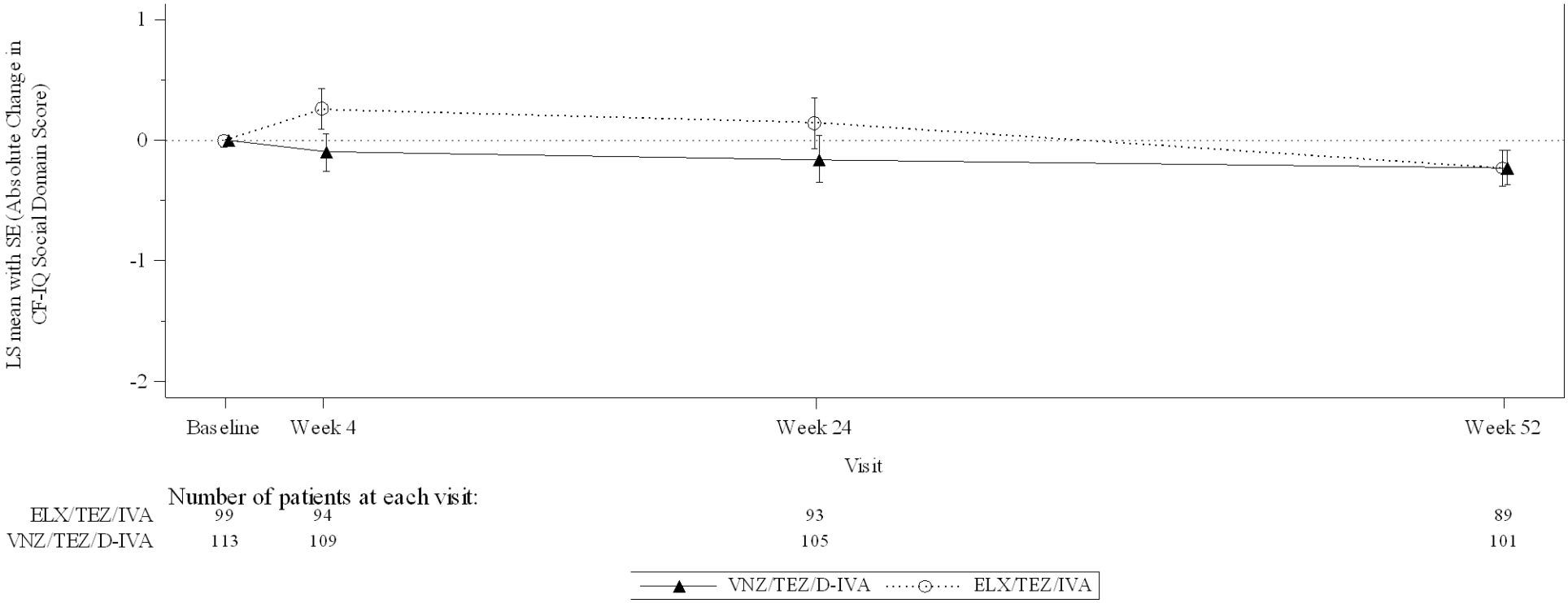
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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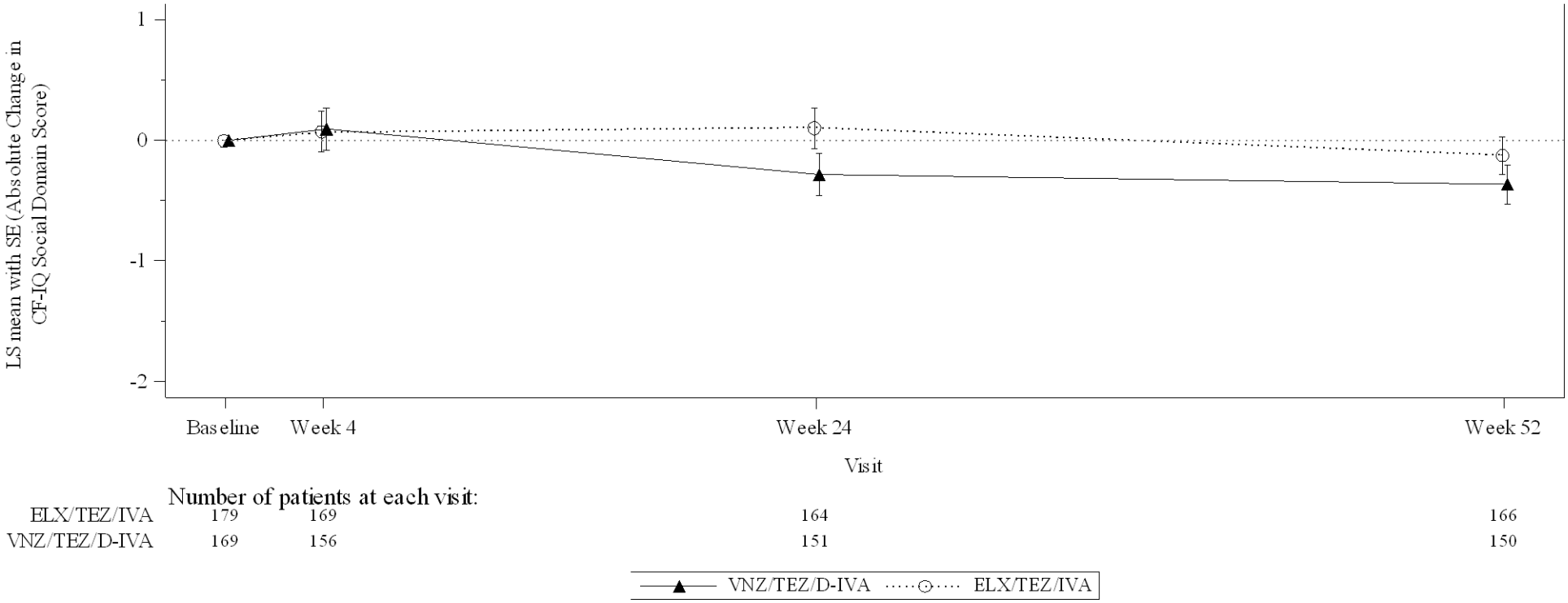
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Social
Region = Rest of World



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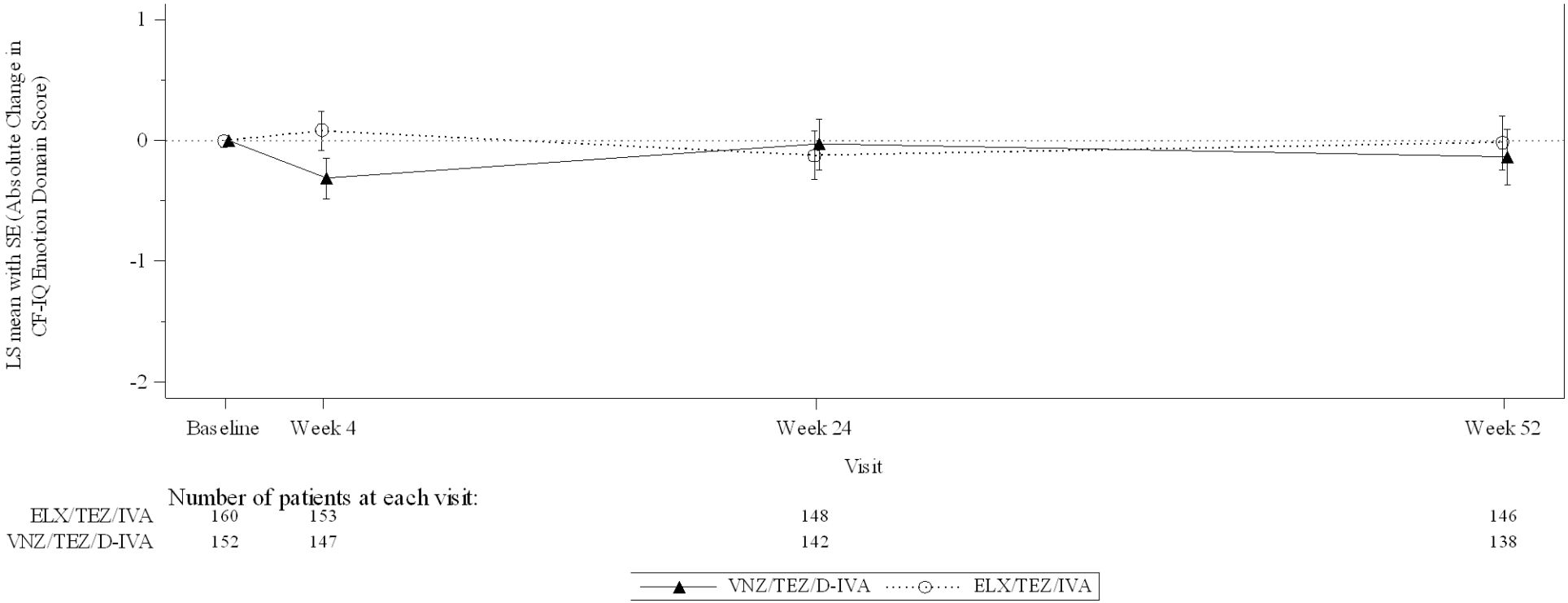
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
ppFEV$_1$ at baseline <70 %



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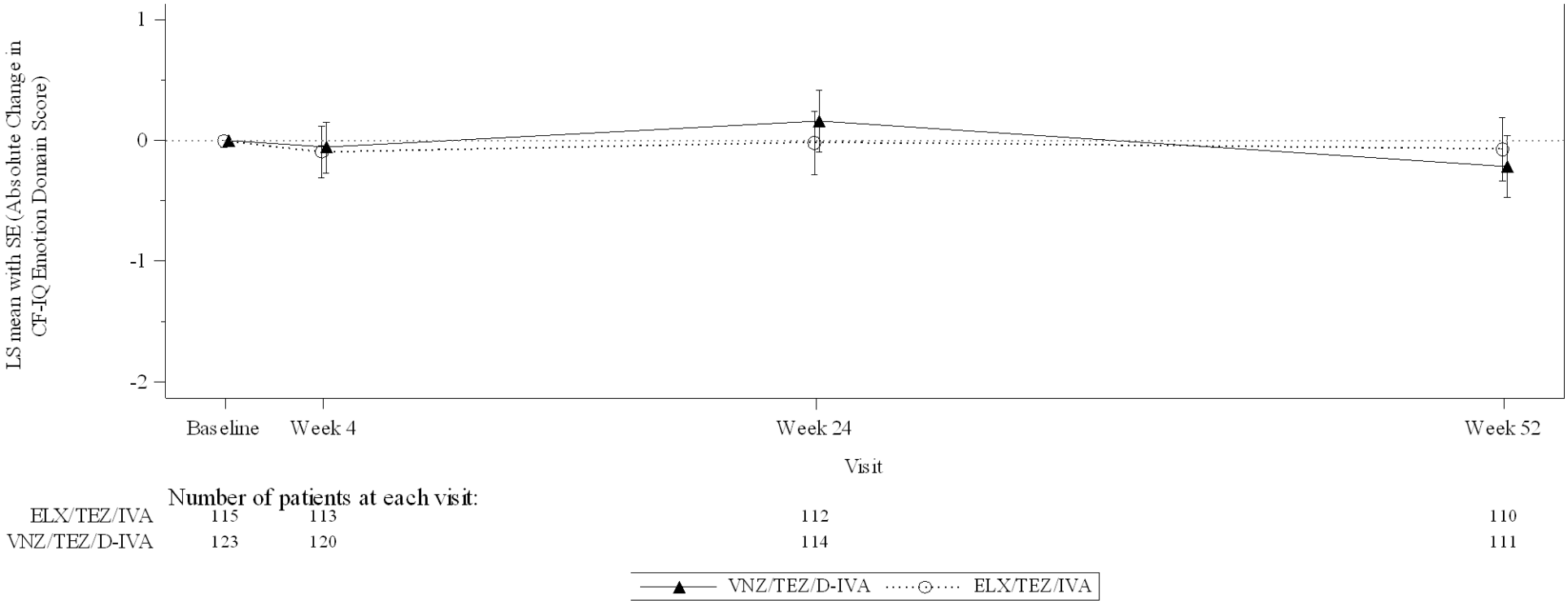
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
ppFEV$_1$ at baseline ≥70 %



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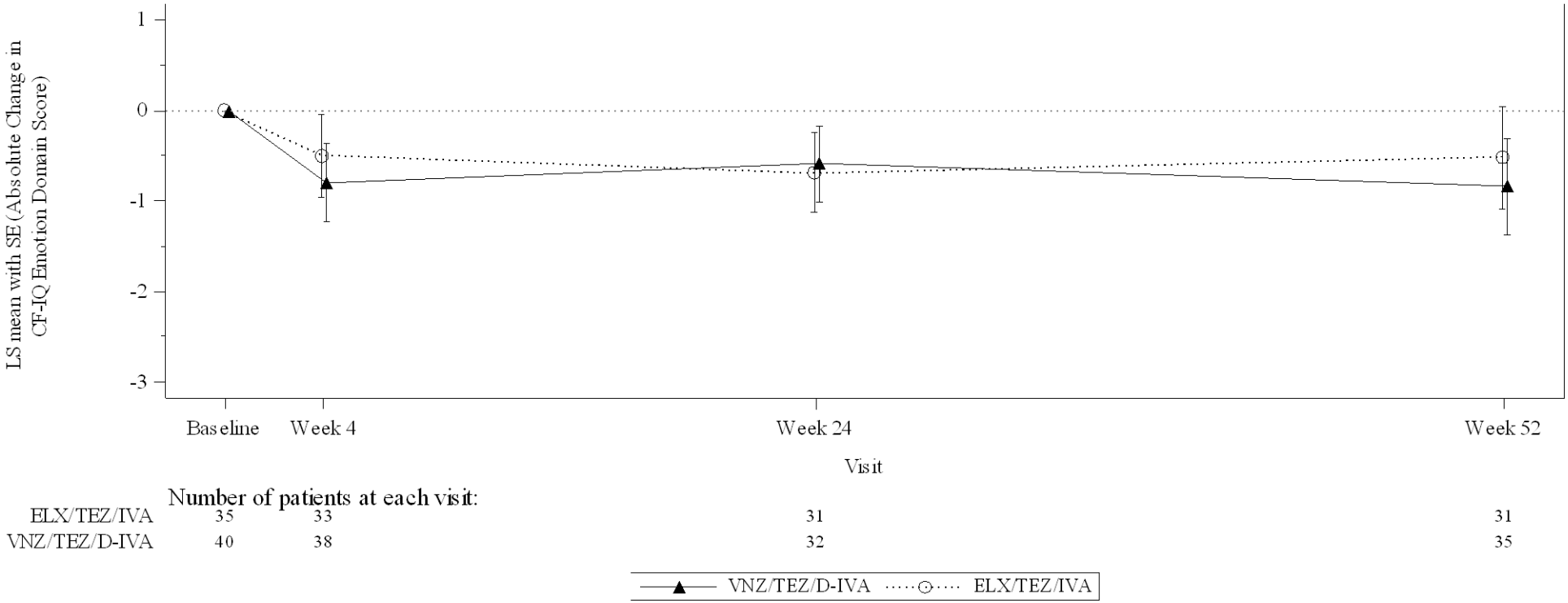
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
Age at screening <18 years



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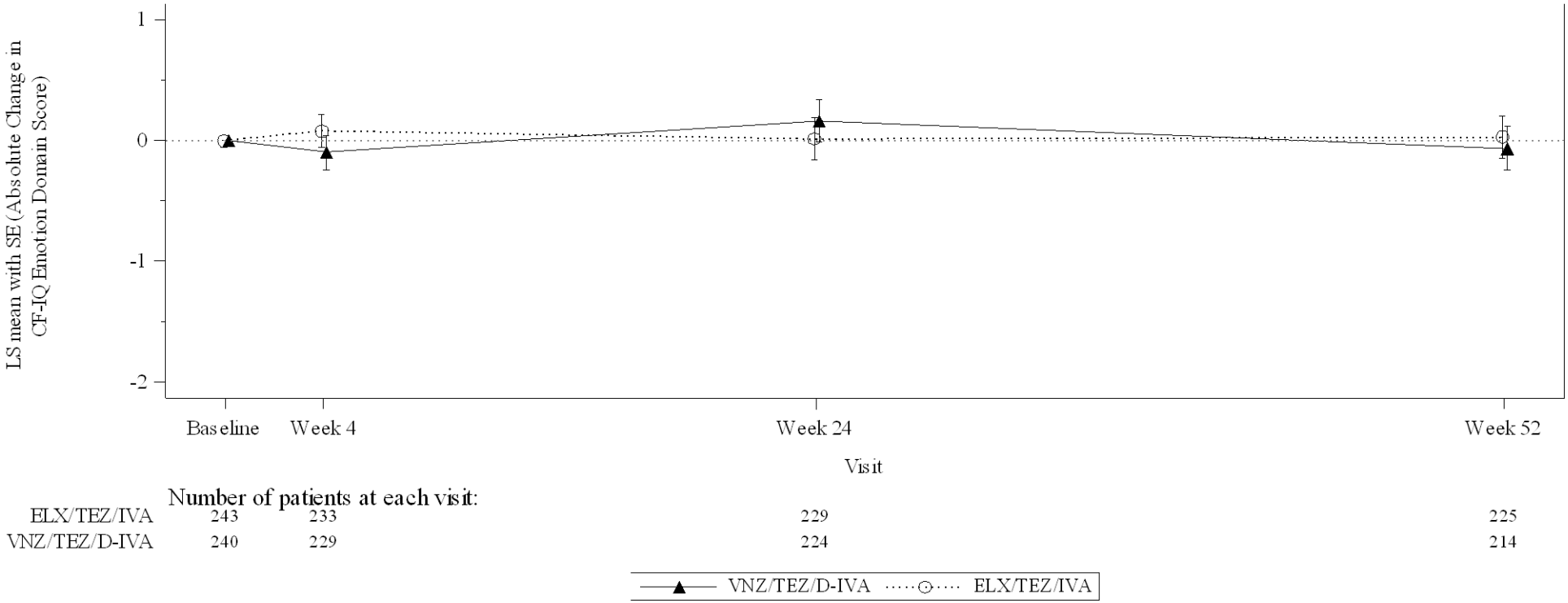
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
Age at screening ≥18 years



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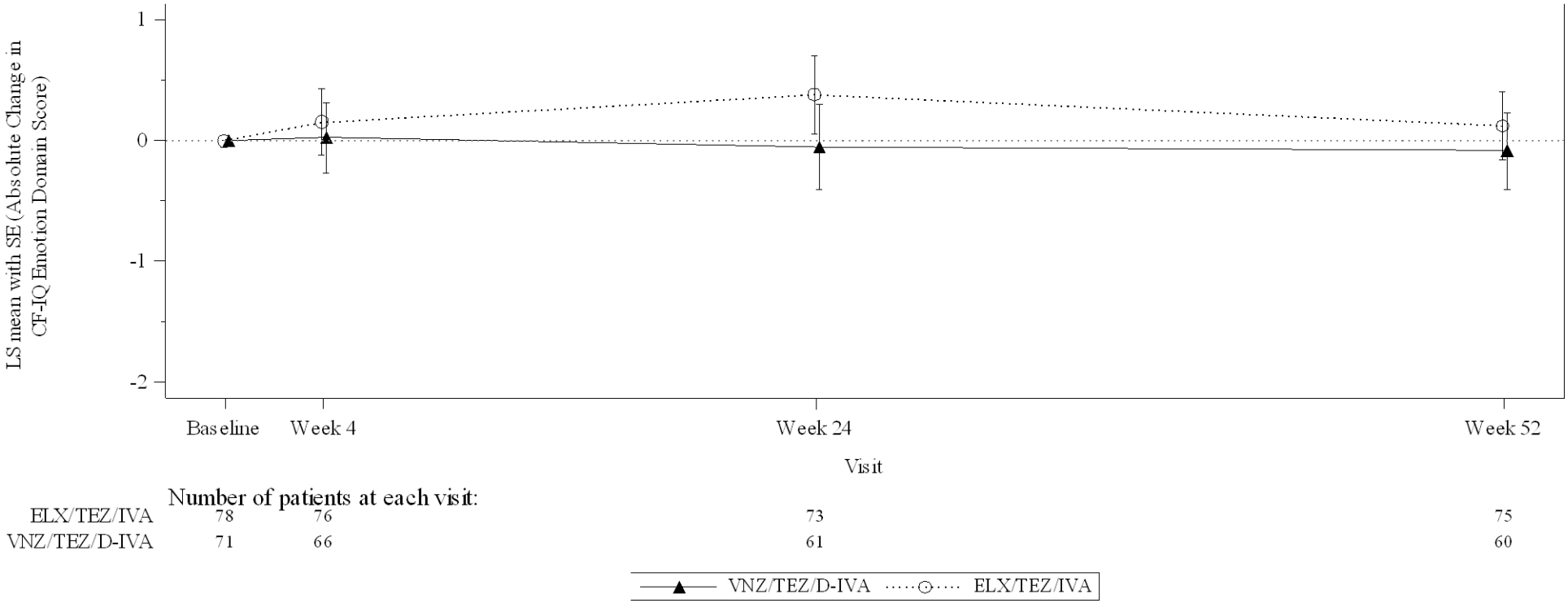
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
SwCl at baseline <30 mmol/L



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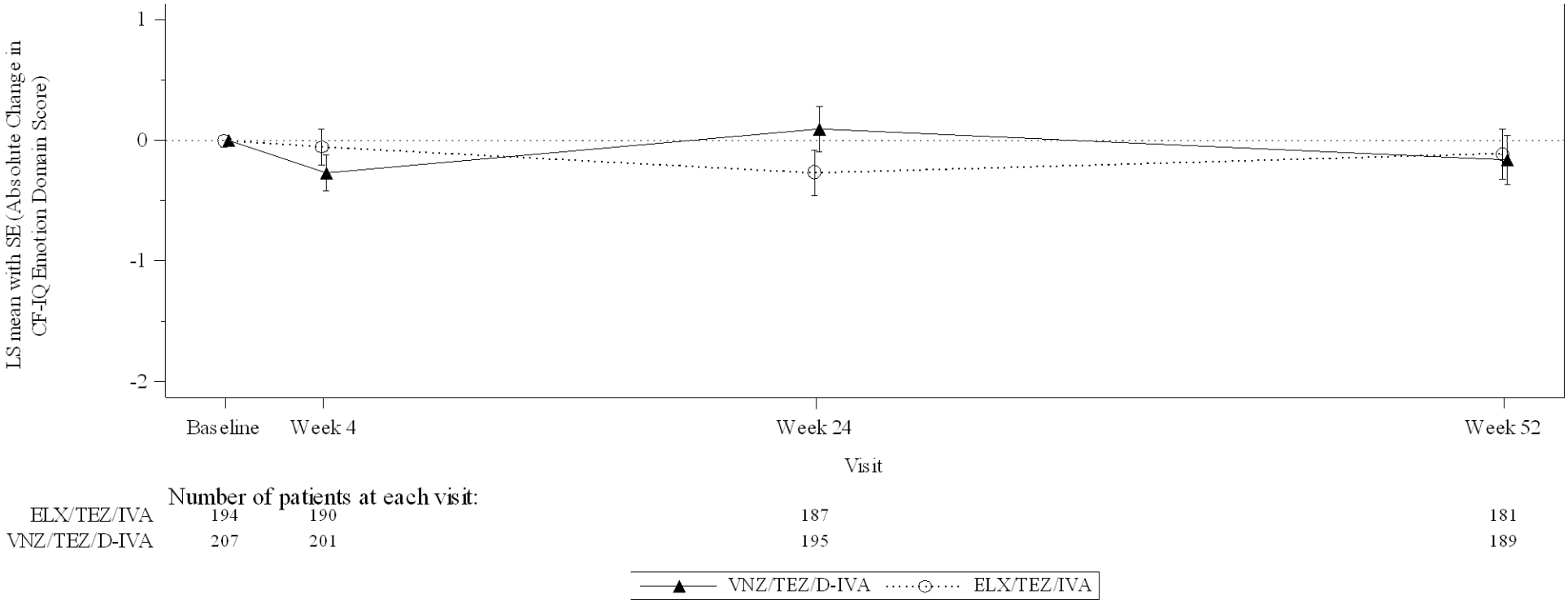
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
SwCl at baseline ≥30 mmol/L



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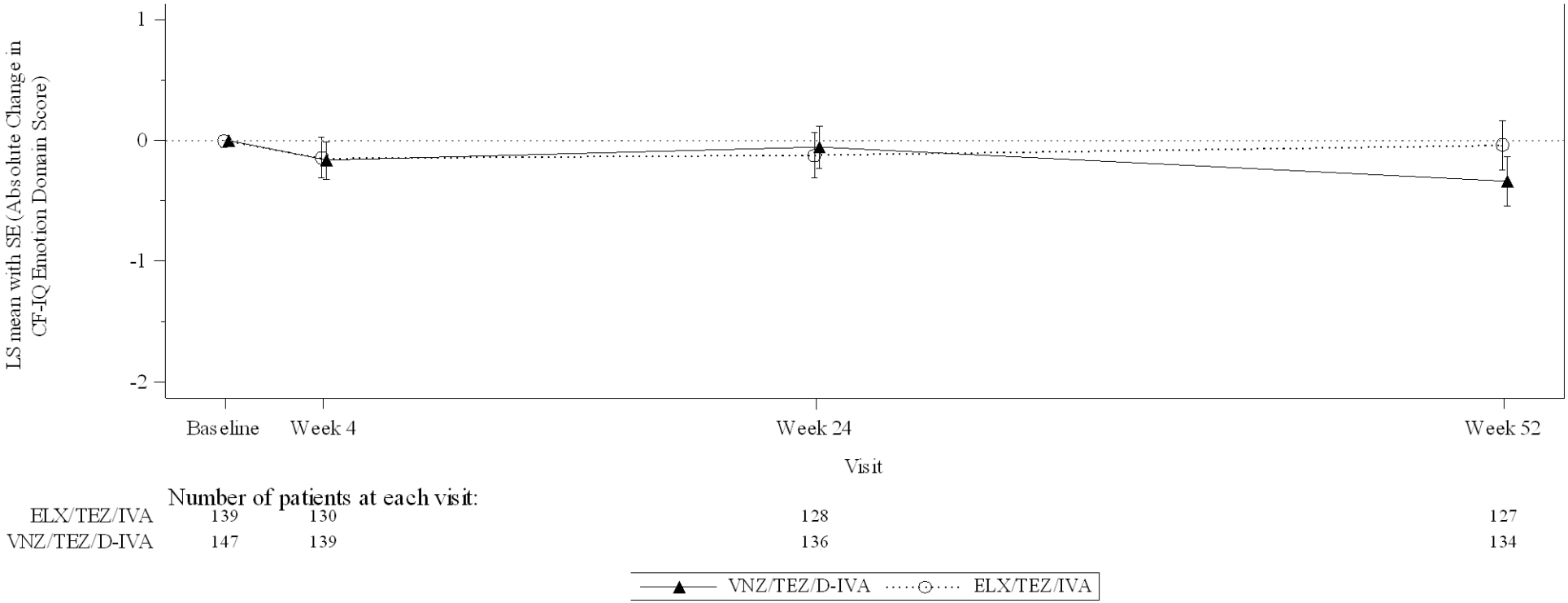
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
Sex = Male



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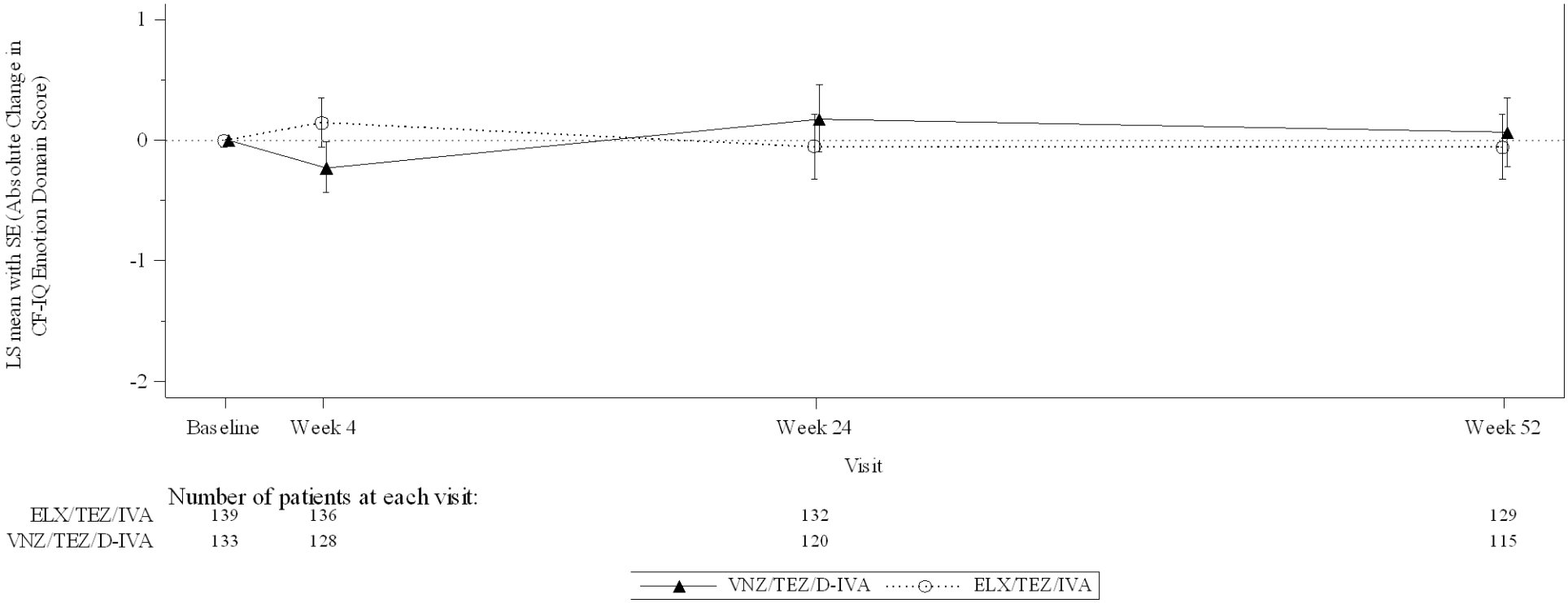
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
Sex = Female



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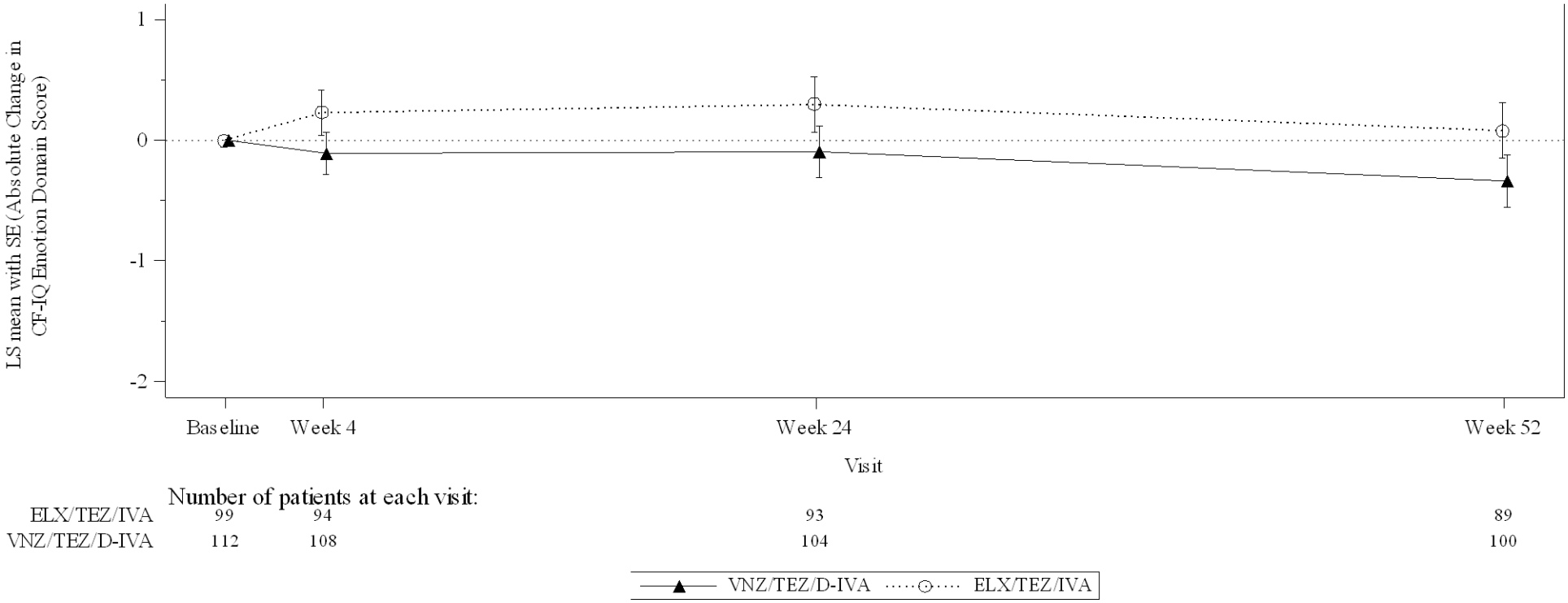
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
Region = North America



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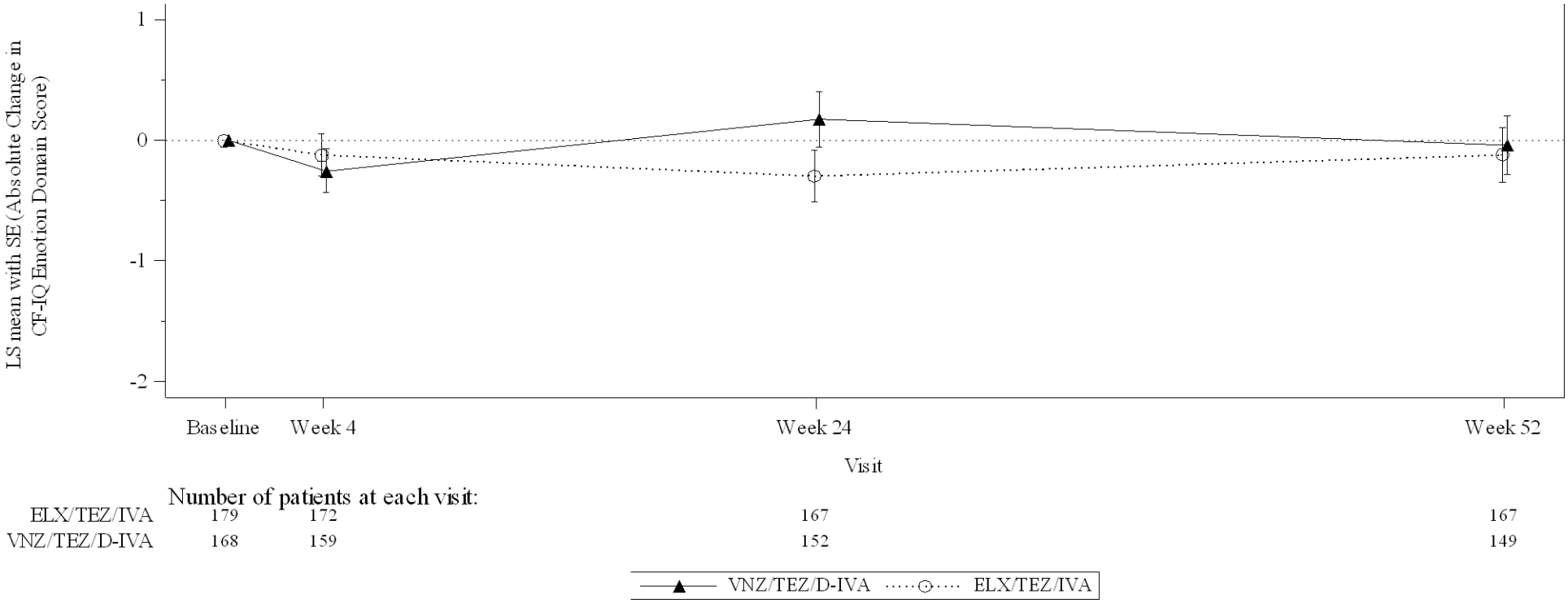
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Emotion
Region = Rest of World



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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
ppFEV$_1$ at baseline <70 %

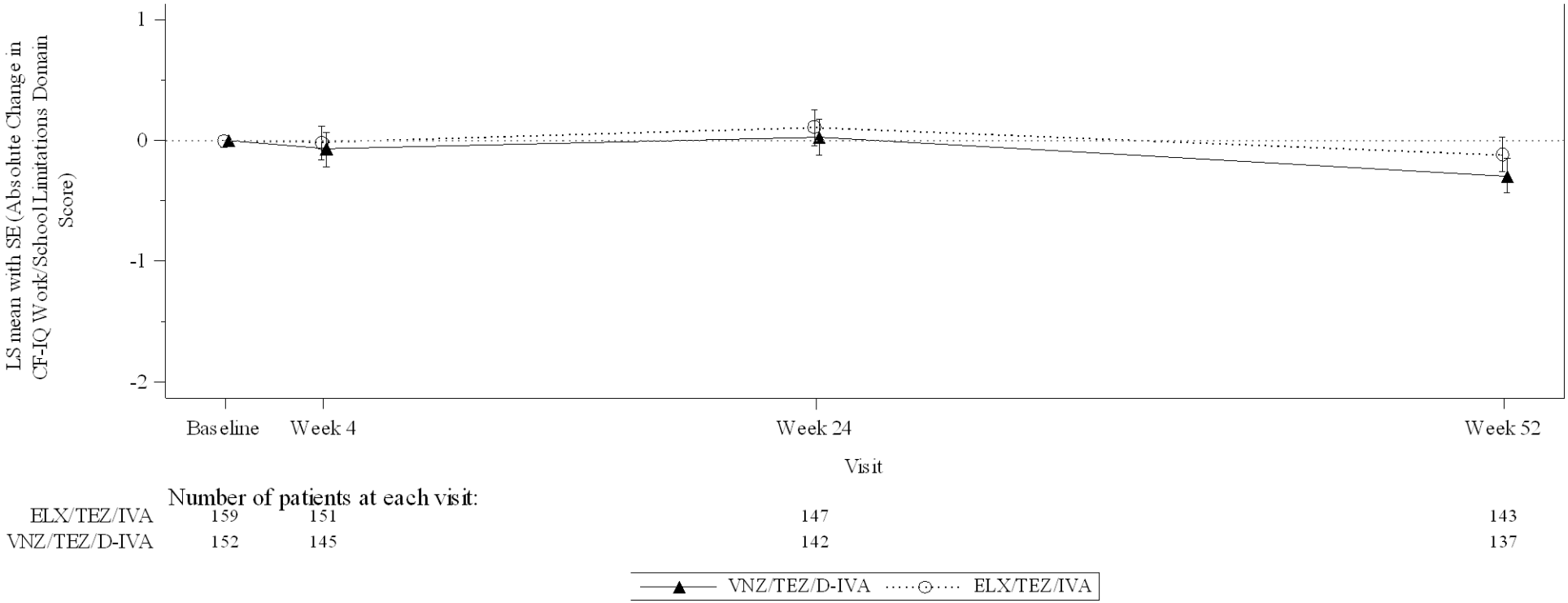

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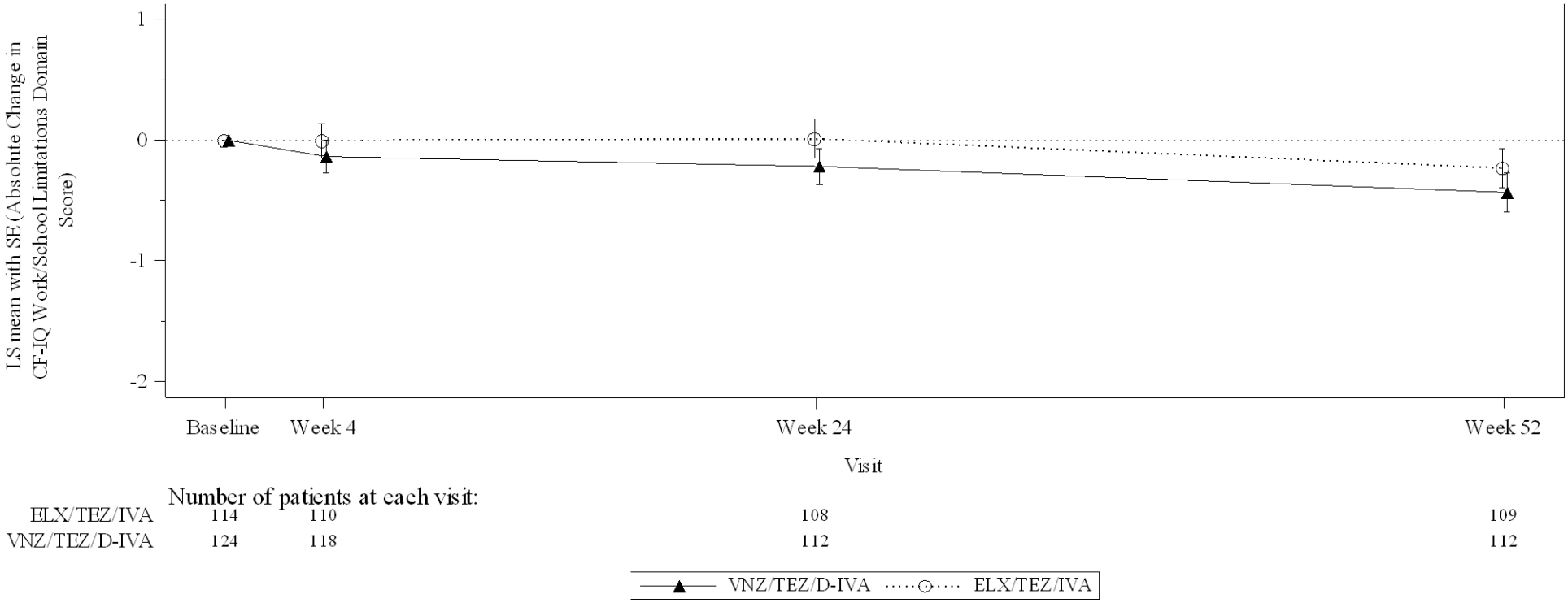
Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
ppFEV$_1$ at baseline ≥70 %



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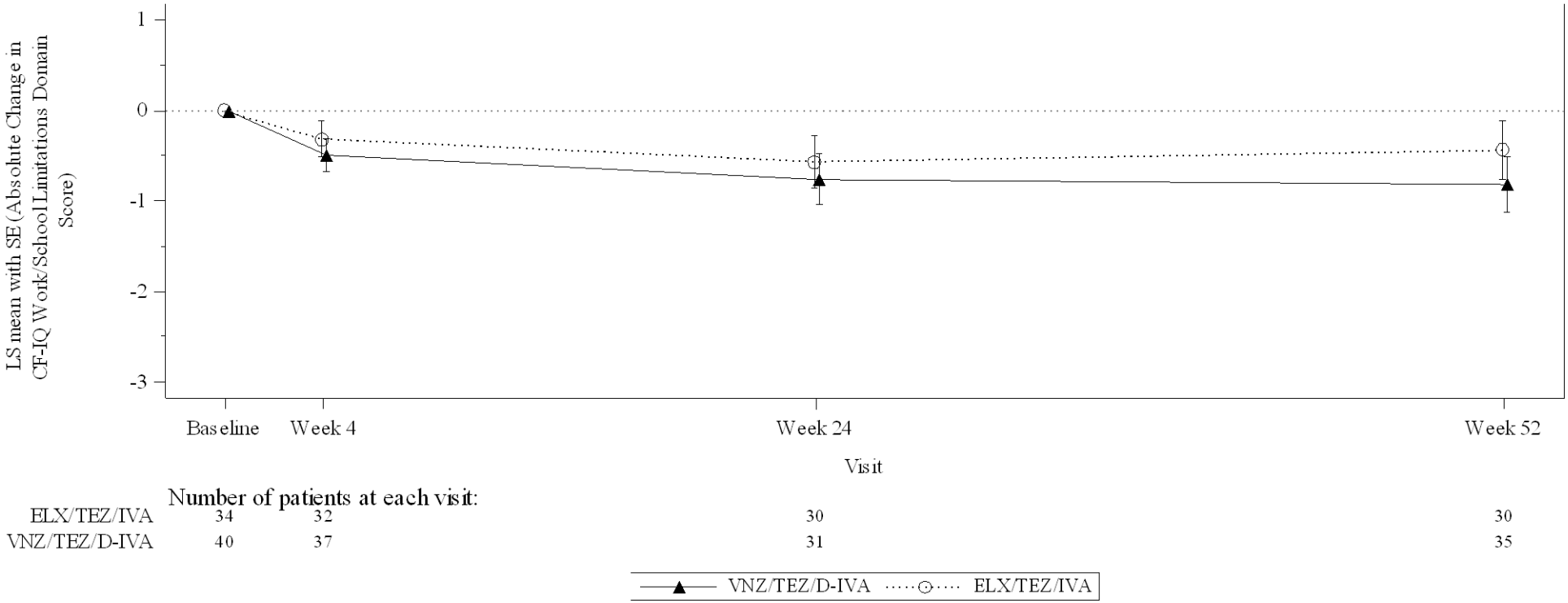
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
Age at screening <18 years



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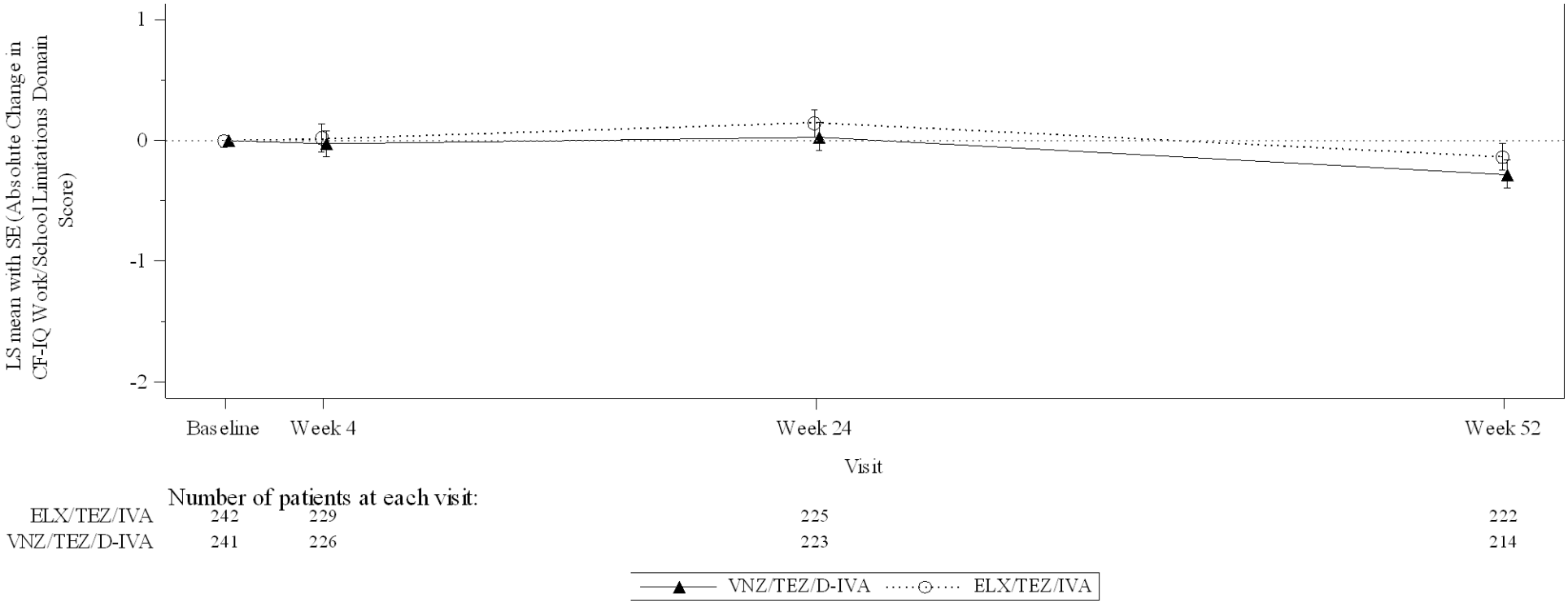
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
Age at screening ≥18 years



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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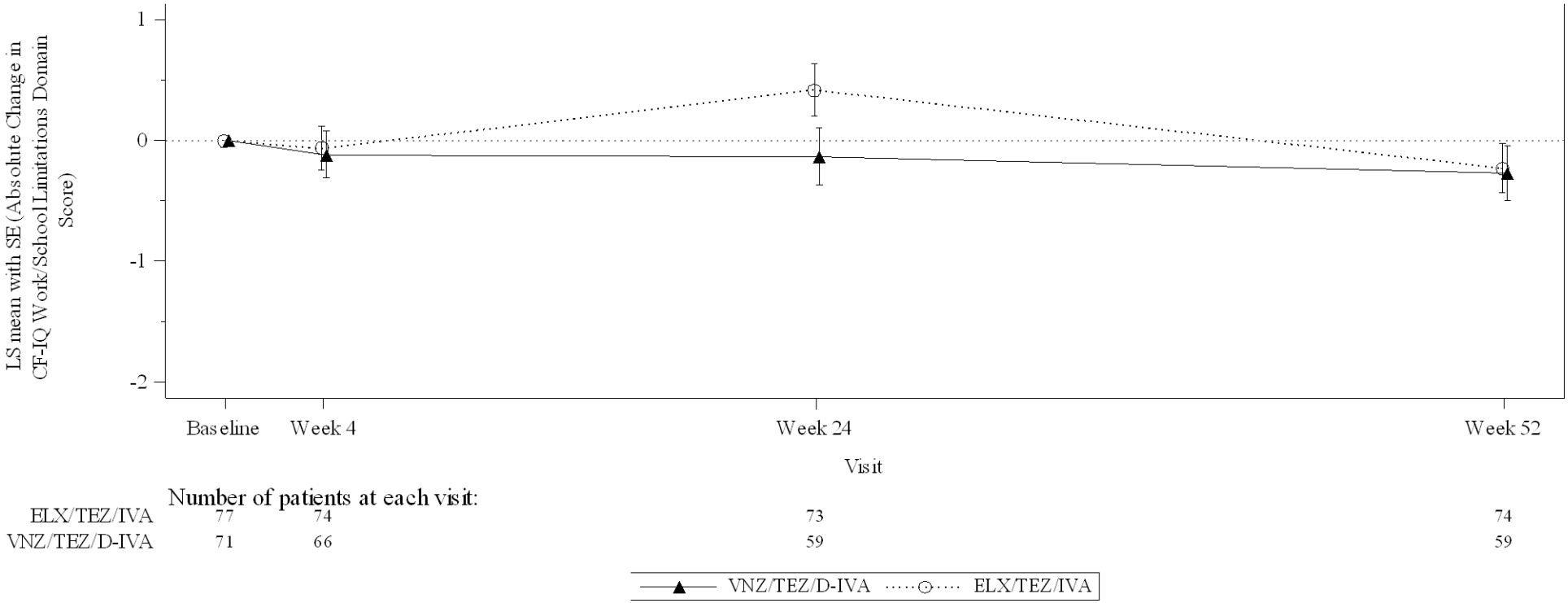
Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
SwCl at baseline <30 mmol/L



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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
SwCl at baseline ≥30 mmol/L

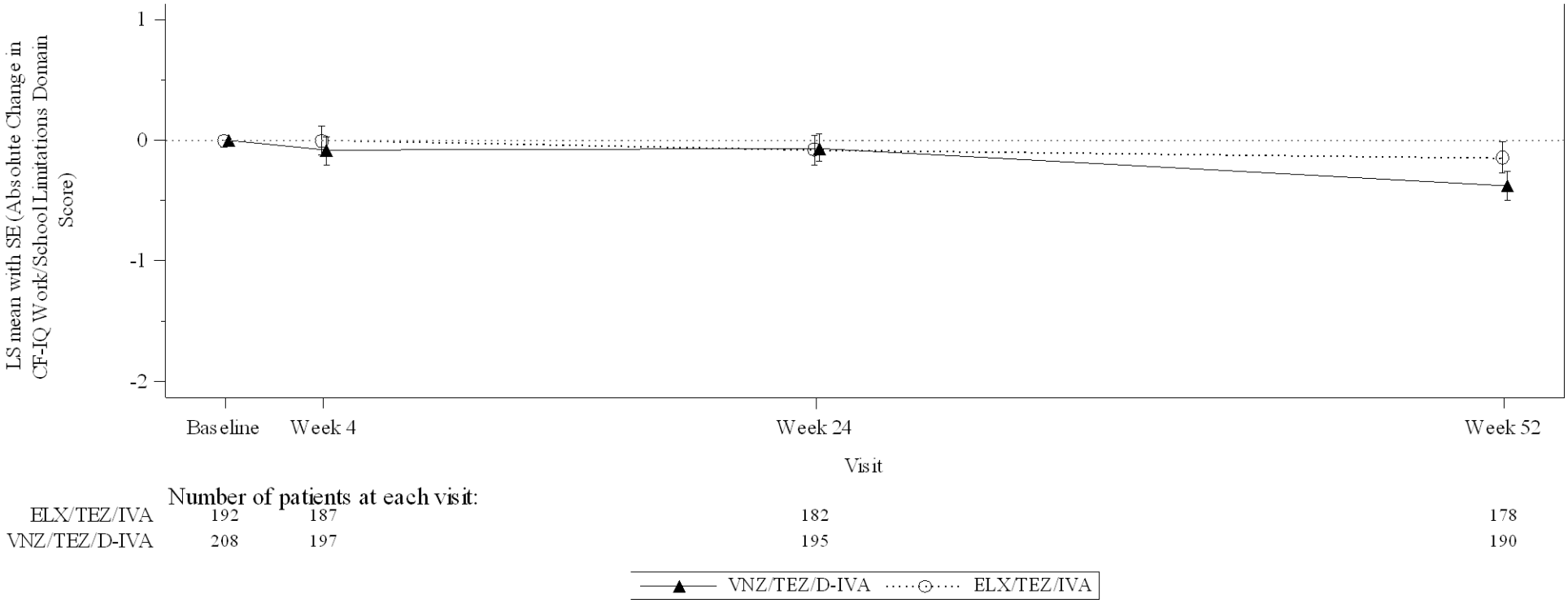

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Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
Sex = Male

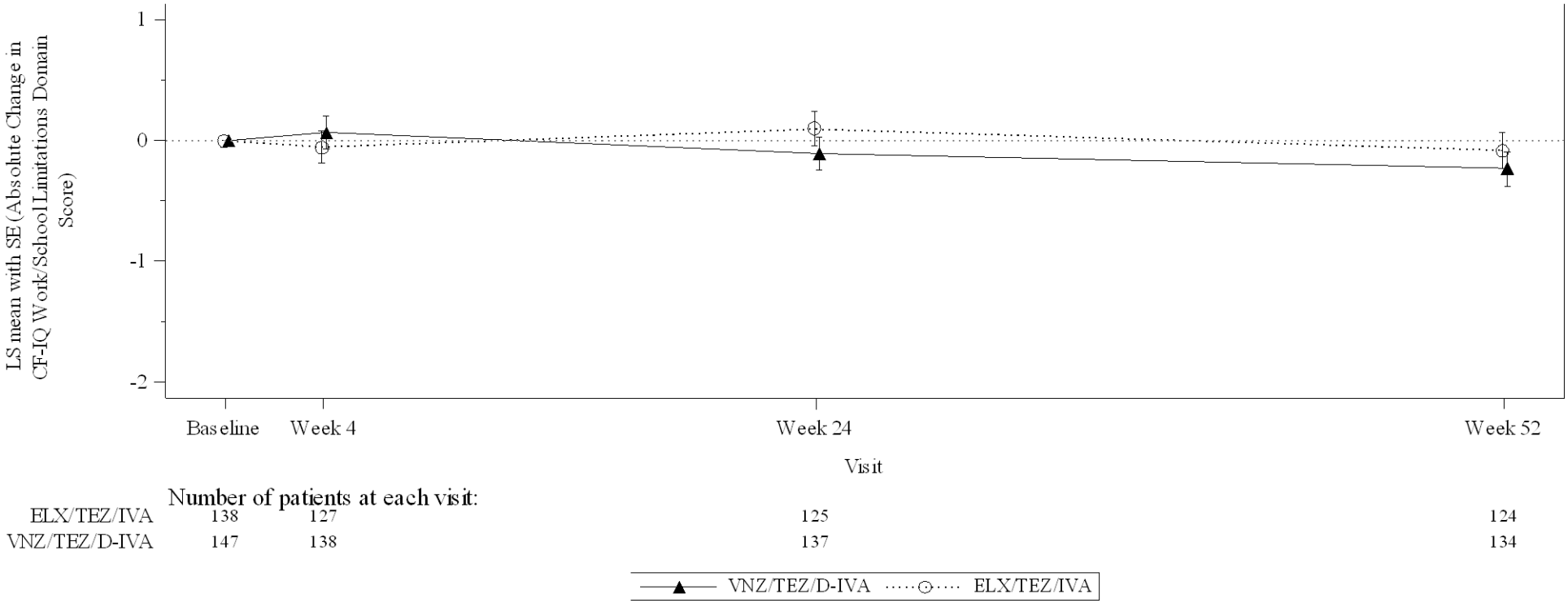

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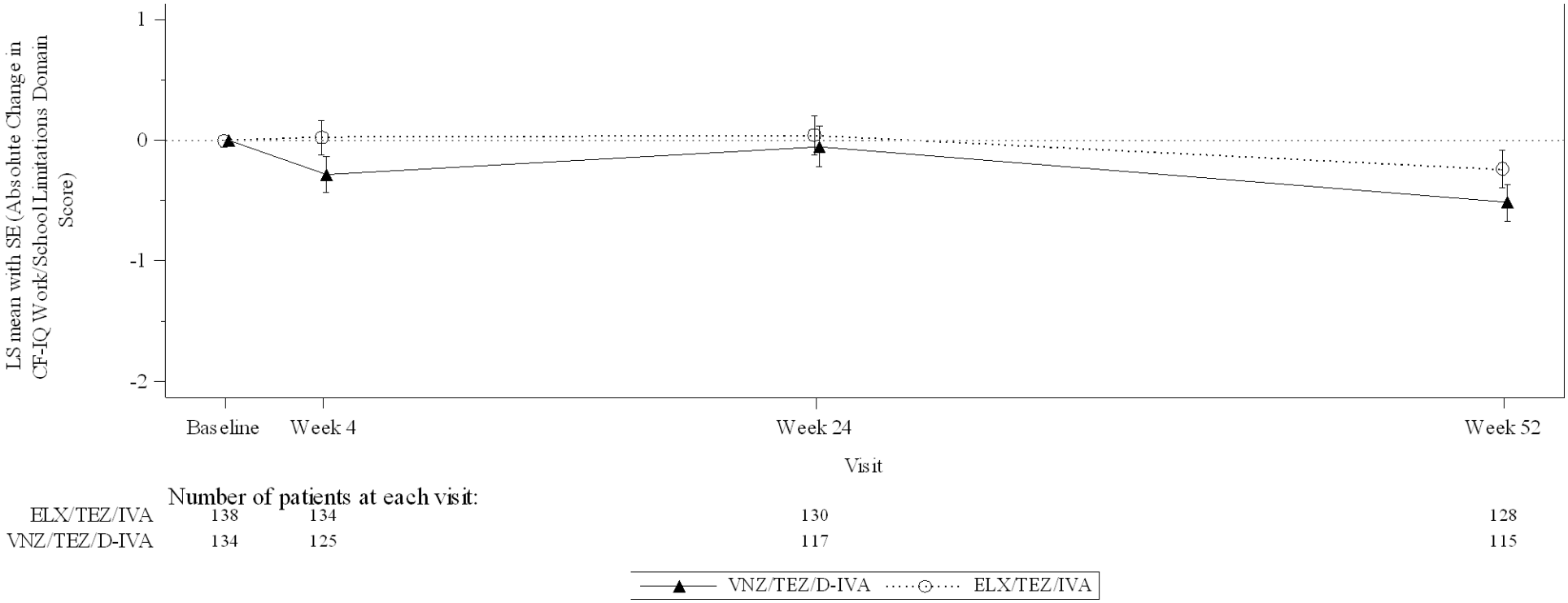
Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
Sex = Female



Number of patients at each visit:

	Baseline	Week 4	Week 24	Week 52
ELX/TEZ/IVA	138	134	130	128
VNZ/TEZ/D-IVA	134	125	117	115

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfiq-52wks-sub-103.sas Creation: 07JAN2025 11:43

Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
Region = North America

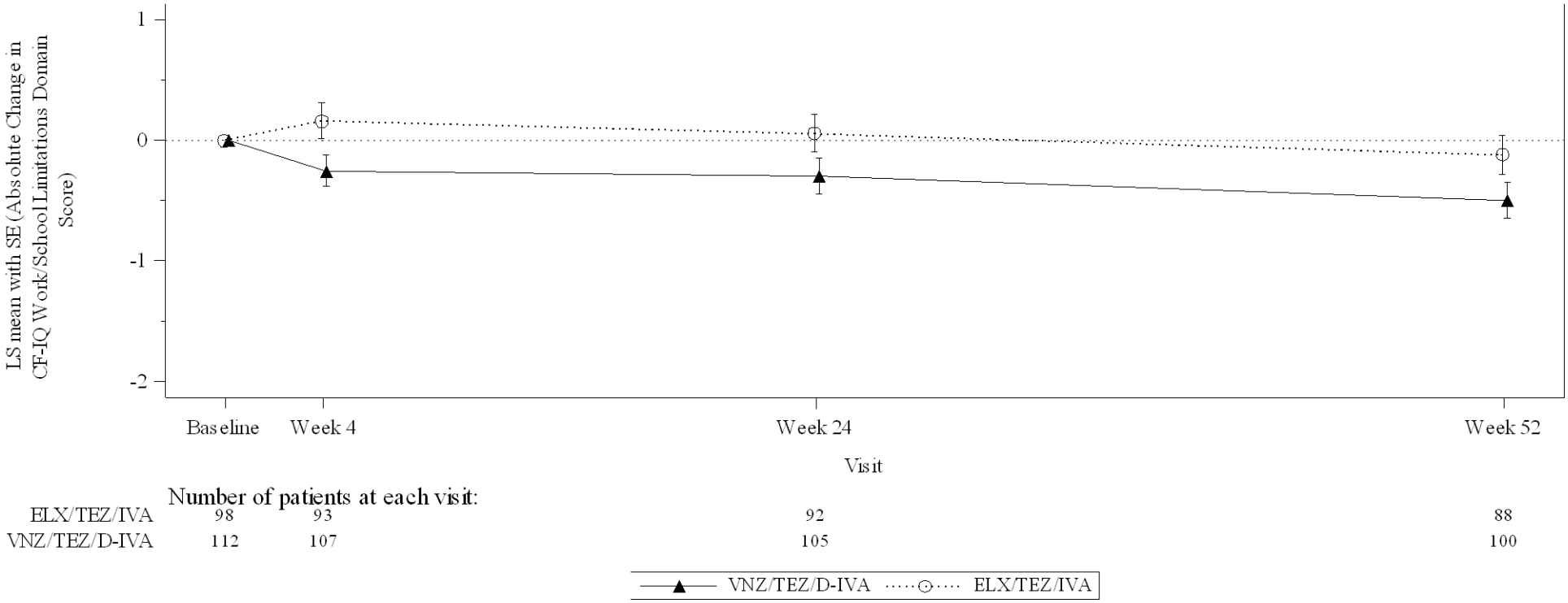

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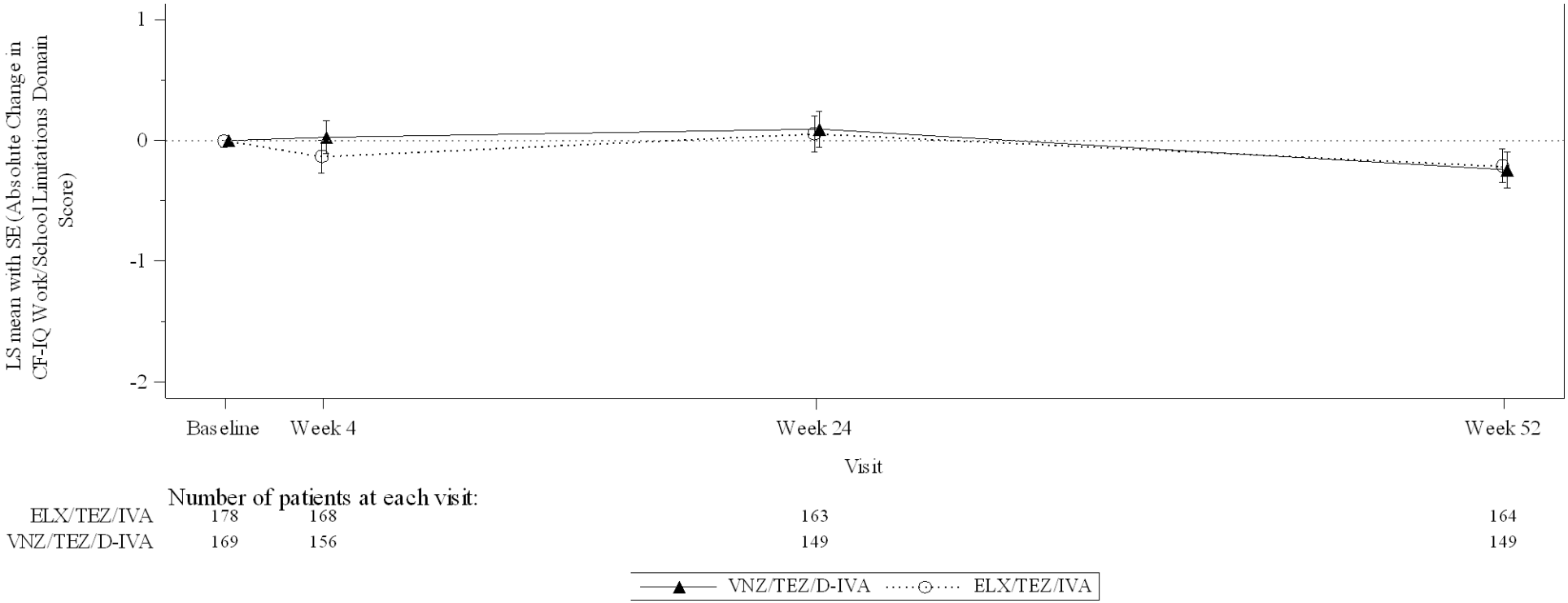
Figure 2.2.2.13.2
Study VX20-121-103: Plot of Absolute Change from Baseline in CF-IQ Domain Score at Each Visit up to Week 52
Full Analysis Set

Domain: Work/School Limitations
Region = Rest of World



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Zusatzanalysen Studie VX21-121-105

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Table 3.3.2.6.1 Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Creatine Kinase Events Safety Set

Table 3.3.2.6.2 Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor Safety Set Sex = Male

Table 3.3.2.7.1 Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Rash Events Safety Set

Table 3.3.2.7.2 Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor Safety Set Sex = Male

Table 3.3.2.8.1 Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Cataract Events Safety Set

Table 3.3.2.8.2 Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor Safety Set Sex = Male

Table 3.3.2.9.1 Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Hypoglycemia Events Safety Set

Table 3.3.2.9.2 Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor Safety Set Sex = Male

Table 3.3.2.10.1 Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Neuropsychiatric Events Safety Set

Table 3.3.2.10.2 Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor Safety Set Sex = Male

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Table 3.3.2.12.1 Study VX21-121-105: Subgroup Factor Test for Treatment-emergent Infective Pulmonary Exacerbation Events Safety Set

Table 3.3.2.12.2 Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor Safety Set Sex = Male

Figure 1.2.1.10.5 Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 for F/MF Full Analysis Set Domain: Respiration

Figure 1.2.1.10.6 Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF Full Analysis Set Domain: Respiration (Parents/Caregivers Form)

Figure 1.2.1.14.2 Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 24 for F/MF Full Analysis Set

Figure 1.2.1.15.2 Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 24 for F/MF Full Analysis Set

Figure 1.2.1.16.2 Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics through Week 24 for F/MF Full Analysis Set

Figure 1.2.2.10.5 Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF Full Analysis Set Domain: Respiration Sex = Male

Figure 1.2.2.10.6 Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF Full Analysis Set Domain: Respiration (Parents/Caregivers Form) Sex = Male

Figure 1.2.2.14.3 Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF Full Analysis Set Sex = Male

Figure 1.2.2.15.3 Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF Full Analysis Set Sex = Male

Figure 1.2.2.16.3 Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF Full Analysis Set Sex = Male

Figure 2.2.1.10.5 Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 non-(F/MF) Full Analysis Set Domain: Respiration

Figure 2.2.1.10.6 Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF) Full Analysis Set Domain: Respiration (Parents/Caregivers Form)

Figure 2.2.1.14.2 Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 24 non-(F/MF) Full Analysis Set

Figure 2.2.1.15.2 Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 24 non-(F/MF) Full Analysis Set

Figure 2.2.1.16.2 Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics through Week 24 non-(F/MF) Full Analysis Set

Figure 2.2.2.10.5 Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups non-(F/MF) Full Analysis Set Domain: Respiration Sex = Male

Figure 2.2.2.10.6 Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups non-(F/MF) Full Analysis Set Domain: Respiration (Parents/Caregivers Form) Sex = Male

Figure 2.2.2.14.3 Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF) Full Analysis Set Sex = Male

Figure 2.2.2.15.3 Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF) Full Analysis Set Sex = Male

Figure 2.2.2.16.3 Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF) Full Analysis Set Sex = Male

Figure 3.2.1.10.5 Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 Full Analysis Set Domain: Respiration

Figure 3.2.1.10.6 Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 Full Analysis Set Domain: Respiration (Parents/Caregivers Form)

Figure 3.2.1.14.2 Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 24 Full Analysis Set

Figure 3.2.1.15.2 Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 24 Full Analysis Set

Figure 3.2.1.16.2 Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics through Week 24 Full Analysis Set

Figure 3.2.2.10.5 Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups Full Analysis Set Domain: Respiration Sex = Male

Figure 3.2.2.10.6 Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups Full Analysis Set Domain: Respiration (Parents/Caregivers Form) Sex = Male

Figure 3.2.2.14.3 Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups Full Analysis Set Sex = Male

Figure 3.2.2.15.3 Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups Full Analysis Set Sex = Male

Figure 3.2.2.16.3 Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups Full Analysis Set Sex = Male

Table 1.1.1.1
Study VX21-121-105: Summary of Duration of Observation (Weeks) per Endpoint for F/MF
Full Analysis Set

Duration of observation (weeks)	VNZ/TEZ/D-IVA N = 24
Overall Study Observation Time	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00
$ppFEV_1$ (percentage points)	
n	23
Mean (SD)	22.80 (3.31)
Median	24.00
Min, Max	12.29, 25.00
BMI (kg/m^2)	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00
BMI z-score	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00
Sweat Chloride (mmol/L)	
n	24
Mean (SD)	23.37 (2.24)
Median	24.00
Min, Max	16.14, 25.00

- Observation duration [weeks] is defined as (date of last observation - first date of study drug in the Treatment Period +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results. For $LCI_{2.5}$, observation duration is derived from dates of accepted multiple breath washout results.

Table 1.1.1.1
Study VX21-121-105: Summary of Duration of Observation (Weeks) per Endpoint for F/MF
Full Analysis Set

Duration of observation (weeks)	VNZ/TEZ/D-IVA N = 24
Weight (kg)	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00
Weight z-score	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00
Height (cm)	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00
Height z-score	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00
CFQ-R	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00

- Observation duration [weeks] is defined as (date of last observation - first date of study drug in the Treatment Period +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results. For $LCI_{2.5}$, observation duration is derived from dates of accepted multiple breath washout results.

Table 1.1.1.1
Study VX21-121-105: Summary of Duration of Observation (Weeks) per Endpoint for F/MF
Full Analysis Set

Duration of observation (weeks)	VNZ/TEZ/D-IVA N = 24
Pulmonary Exacerbation	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00
$LCI_{2.5}$	
n	23
Mean (SD)	21.14 (5.84)
Median	24.00
Min, Max	4.14, 25.00
Safety	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00

- Observation duration [weeks] is defined as (date of last observation - first date of study drug in the Treatment Period +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results. For $LCI_{2.5}$, observation duration is derived from dates of accepted multiple breath washout results.

Table 1.1.2.1
Study VX21-121-105: Summary of Patients with Ongoing Antibiotic Medications at Baseline or at Week 24 for F/MF Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline, N1	24
Subjects with 0 ongoing AB	17 (70.83)
Subjects with 1 ongoing AB	4 (16.67)
Subjects with ≥ 2 ongoing AB	3 (12.50)
Subjects with ≥ 1 ongoing IV AB	0
Week 24, N1	24
Subjects with 0 ongoing AB	17 (70.83)
Subjects with 1 ongoing AB	5 (20.83)
Subjects with ≥ 2 ongoing AB	2 (8.33)
Subjects with ≥ 1 ongoing IV AB	0

- AB: Antibiotic medications are defined as those medications with the ATC level 2 names of "ANTIBACTERIALS FOR SYSTEMIC USE" and "ANTIMYCOBACTERIALS".
- Antibiotic medications included in this summary refer to those with route being "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- IV antibiotic medications refer to those with route being "INTRAVENOUS" or "INTRAVENOUS BOLUS".
- The ongoing antibiotic medications at baseline refer to those with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing antibiotic medications at Week 24 refer to those with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 1.1.2.2
Study VX21-121-105: Summary of Patients with Antibiotic Medications during the Study Treatment Period for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
All subjects	24
Subjects with 0 AB	3 (12.50)
Subjects with 1-3 AB	16 (66.67)
Subjects with ≥ 4 AB	5 (20.83)
Subjects with 0 IV AB	22 (91.67)
Subjects with 1 IV AB	0
Subjects with ≥ 2 IV AB	2 (8.33)
Subjects with 0 ongoing antibiotic medication at baseline	17
Subjects with 0 AB	3 (17.65)
Subjects with 1-3 AB	13 (76.47)
Subjects with ≥ 4 AB	1 (5.88)
Subjects with 0 IV AB	16 (94.12)
Subjects with 1 IV AB	0
Subjects with ≥ 2 IV AB	1 (5.88)

- AB: Antibiotic medications are defined as those medications with the ATC level 2 names of "ANTIBACTERIALS FOR SYSTEMIC USE" and "ANTIMYCOBACTERIALS".
- Antibiotic medications included in this summary refer to those with route being "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- IV antibiotic medications refer to those with route being "INTRAVENOUS" or "INTRAVENOUS BOLUS".
- Antibiotic medications during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period, and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 1.1.3.1
Study VX21-121-105: Summary of Patients with Ongoing Physiotherapies at Baseline or at Week 24 for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline, N1	24
Subjects with 0 ongoing PT	9 (37.50)
Subjects with 1 ongoing PT	13 (54.17)
Subjects with ≥ 2 ongoing PT	2 (8.33)
Week 24, N1	24
Subjects with 0 ongoing PT	9 (37.50)
Subjects with 1 ongoing PT	12 (50.00)
Subjects with ≥ 2 ongoing PT	3 (12.50)

- PT: Physiotherapies refer to the non-pharmacological treatments with preferred names of "Positive expiratory pressure therapy", "Airway secretion clearance therapy", "Positive end-expiratory pressure", or "Physiotherapy chest".
- The ongoing physiotherapy at baseline is defined as a physiotherapy whose start date is prior to first dose date of study drug in the Treatment Period and the end date is ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing physiotherapy at Week 24 is defined as a physiotherapy whose start date is prior to Week 24 visit date and the end date is ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 1.1.3.2
Study VX21-121-105: Summary of Patients with Physiotherapies during the Study Treatment Period for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
All subjects	24
Subjects with 0 PT	9 (37.50)
Subjects with 1 PT	12 (50.00)
Subjects with ≥ 2 PT	3 (12.50)
Subjects with 0 ongoing physiotherapies at baseline	9
Subjects with 0 PT	9 (100.00)
Subjects with 1 PT	0
Subjects with ≥ 2 PT	0

- PT: Physiotherapies refer to the non-pharmacological treatments with preferred names of "Positive expiratory pressure therapy", "Airway secretion clearance therapy", "Positive end-expiratory pressure", or "Physiotherapy chest".
- Physiotherapies during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period, and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 1.1.4.1
Study VX21-121-105: Summary of Patients with Ongoing Inhaled Medications at Baseline or at Week 24 for F/MF Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline, N1	24
Subjects with 0 ongoing IM	2 (8.33)
Subjects with 1 ongoing IM	0
Subjects with ≥ 2 ongoing IM	22 (91.67)
Week 24, N1	24
Subjects with 0 ongoing IM	2 (8.33)
Subjects with 1 ongoing IM	0
Subjects with ≥ 2 ongoing IM	22 (91.67)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB) and for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 24 refer to those IMs with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 1.1.4.2
Study VX21-121-105: Summary of Patients with Inhaled Medications during the Study Treatment Period for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
All subjects	24
Subjects with 0 IM	1 (4.17)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	23 (95.83)
Subjects with 0 ongoing inhaled medication at baseline	2
Subjects with 0 IM	1 (50.00)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	1 (50.00)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB) and for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 1.1.4.3
Study VX21-121-105: Summary of Patients with Ongoing Inhaled Medications for Mucolytics at Baseline or at Week 24 for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline, N1	24
Subjects with 0 ongoing IM	2 (8.33)
Subjects with 1 ongoing IM	7 (29.17)
Subjects with ≥ 2 ongoing IM	15 (62.50)
Week 24, N1	24
Subjects with 0 ongoing IM	2 (8.33)
Subjects with 1 ongoing IM	7 (29.17)
Subjects with ≥ 2 ongoing IM	15 (62.50)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 24 refer to those IMs with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 1.1.4.4
Study VX21-121-105: Summary of Patients with Inhaled Medications for Mucolytics during the Study Treatment Period for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
All subjects	24
Subjects with 0 IM	2 (8.33)
Subjects with 1 IM	7 (29.17)
Subjects with ≥ 2 IM	15 (62.50)
Subjects with 0 ongoing inhaled medication at baseline	2
Subjects with 0 IM	2 (100.00)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	0

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 1.1.4.5

Study VX21-121-105: Summary of Patients with Ongoing Inhaled Medications for Obstructive Airway Disease at Baseline or at Week 24 for F/MF Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline, N1	24
Subjects with 0 ongoing IM	5 (20.83)
Subjects with 1 ongoing IM	11 (45.83)
Subjects with ≥ 2 ongoing IM	8 (33.33)
Week 24, N1	24
Subjects with 0 ongoing IM	5 (20.83)
Subjects with 1 ongoing IM	12 (50.00)
Subjects with ≥ 2 ongoing IM	7 (29.17)

- IM: Inhaled medications refer to those medications for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 24 refer to those IMs with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 1.1.4.6

Study VX21-121-105: Summary of Patients with Inhaled Medications for Obstructive Airway Disease during the Study Treatment Period for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
All subjects	24
Subjects with 0 IM	4 (16.67)
Subjects with 1 IM	11 (45.83)
Subjects with ≥ 2 IM	9 (37.50)
Subjects with 0 ongoing inhaled medication at baseline	5
Subjects with 0 IM	4 (80.00)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	1 (20.00)

- IM: Inhaled medications refer to those medications for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing..
- The percentages in this table are calculated based on the number of subjects under each category.

Table 1.1.5.1
Study VX21-121-105: Summary of Patients with Ongoing CF-related Medications at Baseline or at Week 24 for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline, N1	24
Subjects with 0 ongoing CF-related medications	0
Subjects with 1 ongoing CF-related medications	1 (4.17)
Subjects with 2 ongoing CF-related medications	0
Subjects with 3 ongoing CF-related medications	3 (12.50)
Subjects with 4 ongoing CF-related medications	4 (16.67)
Subjects with ≥5 ongoing CF-related medications	16 (66.67)
Week 24, N1	24
Subjects with 0 ongoing CF-related medications	0
Subjects with 1 ongoing CF-related medications	1 (4.17)
Subjects with 2 ongoing CF-related medications	0
Subjects with 3 ongoing CF-related medications	3 (12.50)
Subjects with 4 ongoing CF-related medications	3 (12.50)
Subjects with ≥5 ongoing CF-related medications	17 (70.83)

- CF-related medications: CF co-medications are defined as those medications with
o ATC level 2 names of "DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES", "DIGESTIVES, INCL. ENZYMES", "ANTIBACTERIALS FOR SYSTEMIC USE", "DRUGS USED IN DIABETES", "BILE AND LIVER THERAPY", "GENERAL NUTRIENTS";
o or ATC level 3 names of "DRUGS FOR CONSTIPATION", "PROPULSIVES";
o or ATC level 4 names of "MUCOLYTICS".
In addition, the route of administration for "DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES" and "MUCOLYTICS" requires to be "RESPIRATORY (INHALATION)" and the route for "ANTIBACTERIALS FOR SYSTEMIC USE" requires to be "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- The ongoing CF-related medications at baseline refer to those CF-related medications with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing CF-related medications at Week 24 refer to those CF-related medications with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 1.2.1.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	94.25 (21.29)
Week 24	
n	20
Mean (SD)	97.22 (17.68)
Absolute Change at Week 24	
n	20
Mean (SD)	0.38 (7.11)
Absolute Change through Week 24 (MMRM)	
n	22
LS mean (SE)	2.48 (2.11)
95% CI of LS mean	(-2.03, 6.98)
P-value	0.2585

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline ppFEV$_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	16.96 (2.15)
Week 24	
n	24
Mean (SD)	17.12 (2.41)
Absolute Change at Week 24	
n	24
Mean (SD)	0.15 (0.63)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	0.15 (0.13)
95% CI of LS mean	(-0.11, 0.42)
P-value	0.2440

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.1.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	0.08 (0.93)
Week 24	
n	24
Mean (SD)	-0.01 (1.04)
Absolute Change at Week 24	
n	24
Mean (SD)	-0.09 (0.32)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	-0.09 (0.06)
95% CI of LS mean	(-0.22, 0.05)
P-value	0.1882

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.1.4.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	23
Mean (SD)	52.59 (18.88)
Week 24	
n	22
Mean (SD)	42.20 (15.76)
Absolute Change at Week 24	
n	22
Mean (SD)	-11.55 (10.36)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	-10.54 (2.06)
95% CI of LS mean	(-14.82, -6.26)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.4.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Non-missing value at Week 24, N1	22
Number of subjects with missing value at Week 24	2
SwCl <60 mmol/L at Week 24, n (%)	18 (75.00)
95% CI for the proportion	(53.29, 90.23)

- N1: number of subjects with non-missing SwCl at Week 24
- n: number of subjects with SwCl <60 mmol/L
- 95% CI is based on the Clopper-Pearson method

Table 1.2.1.4.3
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Non-missing value at Week 24, N1	22
Number of subjects with missing value at Week 24	2
SwCl <30 mmol/L at Week 24, n (%)	5 (20.83)
95% CI for the proportion	(7.13, 42.15)

- N1: number of subjects with non-missing SwCl at Week 24
- n: number of subjects with SwCl <30 mmol/L
- 95% CI is based on the Clopper-Pearson method

Table 1.2.1.5
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	30.73 (5.58)
Week 24	
n	24
Mean (SD)	32.34 (6.19)
Absolute Change at Week 24	
n	24
Mean (SD)	1.61 (1.30)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	1.61 (0.27)
95% CI of LS mean	(1.05, 2.17)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.1.6
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	0.00 (0.87)
Week 24	
n	24
Mean (SD)	-0.04 (0.96)
Absolute Change at Week 24	
n	24
Mean (SD)	-0.04 (0.22)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	-0.04 (0.04)
95% CI of LS mean	(-0.13, 0.06)
P-value	0.4348

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.1.7
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	134.30 (9.31)
Week 24	
n	24
Mean (SD)	137.13 (9.47)
Absolute Change at Week 24	
n	24
Mean (SD)	2.83 (0.99)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	2.83 (0.20)
95% CI of LS mean	(2.41, 3.25)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.1.8
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	-0.07 (0.93)
Week 24	
n	24
Mean (SD)	-0.04 (0.94)
Absolute Change at Week 24	
n	24
Mean (SD)	0.03 (0.15)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	0.03 (0.03)
95% CI of LS mean	(-0.03, 0.09)
P-value	0.2782

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.1.9
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	21
Mean (SD)	6.92 (1.06)
Week 24	
n	17
Mean (SD)	6.47 (0.61)
Absolute Change at Week 24	
n	16
Mean (SD)	-0.24 (0.62)
Absolute Change through Week 24 (MMRM)	
n	16
LS mean (SE)	-0.12 (0.09)
95% CI of LS mean	(-0.33, 0.08)
P-value	0.2140

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 1.2.1.10.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	23
Mean (SD)	89.86 (7.93)
Week 4 (MMRM)	
n	23
LS mean (SE)	90.22 (1.85)
95% CI of LS mean	(86.38, 94.05)
Absolute Change at Week 4 (MMRM)	
n	23
LS mean (SE)	0.36 (1.85)
95% CI of LS mean	(-3.47, 4.20)
Week 8 (MMRM)	
n	23
LS mean (SE)	89.49 (2.42)
95% CI of LS mean	(84.47, 94.52)
Absolute Change at Week 8 (MMRM)	
n	23
LS mean (SE)	-0.36 (2.42)
95% CI of LS mean	(-5.39, 4.66)
Week 12 (MMRM)	
n	23
LS mean (SE)	91.67 (1.82)
95% CI of LS mean	(87.89, 95.44)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.1.10.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Absolute Change at Week 12 (MMRM)	
n	23
LS mean (SE)	1.81 (1.82)
95% CI of LS mean	(-1.96, 5.59)
Week 16 (MMRM)	
n	23
LS mean (SE)	91.67 (1.79)
95% CI of LS mean	(87.95, 95.38)
Absolute Change at Week 16 (MMRM)	
n	23
LS mean (SE)	1.81 (1.79)
95% CI of LS mean	(-1.90, 5.53)
Week 24	
n	24
Mean (SD)	89.24 (10.56)
Absolute Change at Week 24	
n	23
Mean (SD)	-0.72 (10.63)
Week 24 (MMRM)	
n	24
LS mean (SE)	89.13 (2.10)
95% CI of LS mean	(84.77, 93.49)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Absolute Change at Week 24 (MMRM)	
n	23
LS mean (SE)	-0.72 (2.10)
95% CI of LS mean	(-5.09, 3.64)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	0.54 (1.46)
95% CI of LS mean	(-2.49, 3.57)
P-value	0.7134

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Respiration

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	23 (95.83)
Week 4	23 (95.83)
Absolute Change at Week 4	23 (95.83)
Week 8	23 (95.83)
Absolute Change at Week 8	23 (95.83)
Week 12	23 (95.83)
Absolute Change at Week 12	23 (95.83)
Week 16	23 (95.83)
Absolute Change at Week 16	23 (95.83)
Week 24	24 (100.00)
Absolute Change at Week 24	23 (95.83)
Through Week 24	24 (100.00)
Absolute Change through Week 24	23 (95.83)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	23 (95.83)
Week 4	23 (95.83)
Absolute Change at Week 4	23 (95.83)
Week 8	23 (95.83)
Absolute Change at Week 8	23 (95.83)
Week 12	23 (95.83)
Absolute Change at Week 12	23 (95.83)
Week 16	23 (95.83)
Absolute Change at Week 16	23 (95.83)
Week 24	24 (100.00)
Absolute Change at Week 24	23 (95.83)
Through Week 24	24 (100.00)
Absolute Change through Week 24	23 (95.83)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	23 (95.83)
Week 4	23 (95.83)
Absolute Change at Week 4	23 (95.83)
Week 8	23 (95.83)
Absolute Change at Week 8	23 (95.83)
Week 12	23 (95.83)
Absolute Change at Week 12	23 (95.83)
Week 16	23 (95.83)
Absolute Change at Week 16	23 (95.83)
Week 24	24 (100.00)
Absolute Change at Week 24	23 (95.83)
Through Week 24	24 (100.00)
Absolute Change through Week 24	23 (95.83)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	23 (95.83)
Week 4	23 (95.83)
Absolute Change at Week 4	23 (95.83)
Week 8	23 (95.83)
Absolute Change at Week 8	23 (95.83)
Week 12	23 (95.83)
Absolute Change at Week 12	23 (95.83)
Week 16	23 (95.83)
Absolute Change at Week 16	23 (95.83)
Week 24	24 (100.00)
Absolute Change at Week 24	23 (95.83)
Through Week 24	24 (100.00)
Absolute Change through Week 24	23 (95.83)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	23 (95.83)
Week 4	23 (95.83)
Absolute Change at Week 4	23 (95.83)
Week 8	23 (95.83)
Absolute Change at Week 8	23 (95.83)
Week 12	23 (95.83)
Absolute Change at Week 12	23 (95.83)
Week 16	23 (95.83)
Absolute Change at Week 16	23 (95.83)
Week 24	24 (100.00)
Absolute Change at Week 24	23 (95.83)
Through Week 24	24 (100.00)
Absolute Change through Week 24	23 (95.83)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	23 (95.83)
Week 4	23 (95.83)
Absolute Change at Week 4	23 (95.83)
Week 8	23 (95.83)
Absolute Change at Week 8	23 (95.83)
Week 12	23 (95.83)
Absolute Change at Week 12	23 (95.83)
Week 16	23 (95.83)
Absolute Change at Week 16	23 (95.83)
Week 24	24 (100.00)
Absolute Change at Week 24	23 (95.83)
Through Week 24	24 (100.00)
Absolute Change through Week 24	23 (95.83)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Social

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	23 (95.83)
Week 4	23 (95.83)
Absolute Change at Week 4	23 (95.83)
Week 8	23 (95.83)
Absolute Change at Week 8	23 (95.83)
Week 12	23 (95.83)
Absolute Change at Week 12	23 (95.83)
Week 16	23 (95.83)
Absolute Change at Week 16	23 (95.83)
Week 24	24 (100.00)
Absolute Change at Week 24	23 (95.83)
Through Week 24	24 (100.00)
Absolute Change through Week 24	23 (95.83)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	23 (95.83)
Week 4	23 (95.83)
Absolute Change at Week 4	23 (95.83)
Week 8	23 (95.83)
Absolute Change at Week 8	23 (95.83)
Week 12	23 (95.83)
Absolute Change at Week 12	23 (95.83)
Week 16	23 (95.83)
Absolute Change at Week 16	23 (95.83)
Week 24	24 (100.00)
Absolute Change at Week 24	23 (95.83)
Through Week 24	24 (100.00)
Absolute Change through Week 24	23 (95.83)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	91.62 (9.40)
Week 4 (MMRM)	
n	24
LS mean (SE)	83.56 (3.09)
95% CI of LS mean	(77.17, 89.96)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	-8.06 (3.09)
95% CI of LS mean	(-14.45, -1.66)
Week 8 (MMRM)	
n	24
LS mean (SE)	86.81 (3.66)
95% CI of LS mean	(79.24, 94.37)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	-4.81 (3.66)
95% CI of LS mean	(-12.38, 2.75)
Week 12 (MMRM)	
n	24
LS mean (SE)	93.06 (1.45)
95% CI of LS mean	(90.05, 96.06)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	1.44 (1.45)
95% CI of LS mean	(-1.57, 4.44)
Week 16 (MMRM)	
n	24
LS mean (SE)	91.90 (2.27)
95% CI of LS mean	(87.19, 96.60)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	0.28 (2.27)
95% CI of LS mean	(-4.43, 4.98)
Week 24	
n	24
Mean (SD)	88.43 (13.50)
Absolute Change at Week 24	
n	24
Mean (SD)	-3.19 (15.75)
Week 24 (MMRM)	
n	24
LS mean (SE)	88.43 (2.79)
95% CI of LS mean	(82.65, 94.21)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	-3.19 (2.79)
95% CI of LS mean	(-8.97, 2.58)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	-1.46 (1.64)
95% CI of LS mean	(-4.85, 1.93)
P-value	0.3824

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Respiration

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Health Perception

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: School

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Vitality

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Weight

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	23
Mean (SD)	90.82 (16.29)
Week 4 (MMRM)	
n	23
LS mean (SE)	91.30 (3.31)
95% CI of LS mean	(84.44, 98.16)
Absolute Change at Week 4 (MMRM)	
n	23
LS mean (SE)	0.48 (3.31)
95% CI of LS mean	(-6.38, 7.34)
Week 8 (MMRM)	
n	23
LS mean (SE)	90.34 (3.56)
95% CI of LS mean	(82.96, 97.72)
Absolute Change at Week 8 (MMRM)	
n	23
LS mean (SE)	-0.48 (3.56)
95% CI of LS mean	(-7.86, 6.90)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	23
LS mean (SE)	90.34 (2.69)
95% CI of LS mean	(84.73, 95.95)
Absolute Change at Week 12 (MMRM)	
n	23
LS mean (SE)	-0.48 (2.69)
95% CI of LS mean	(-6.09, 5.13)
Week 16 (MMRM)	
n	23
LS mean (SE)	94.69 (1.82)
95% CI of LS mean	(90.91, 98.46)
Absolute Change at Week 16 (MMRM)	
n	23
LS mean (SE)	3.86 (1.82)
95% CI of LS mean	(0.09, 7.64)
Week 24	
n	24
Mean (SD)	94.44 (12.26)
Absolute Change at Week 24	
n	23
Mean (SD)	5.31 (15.30)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	96.14 (1.84)
95% CI of LS mean	(92.31, 99.96)
Absolute Change at Week 24 (MMRM)	
n	23
LS mean (SE)	5.31 (1.84)
95% CI of LS mean	(1.49, 9.14)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	4.59 (1.71)
95% CI of LS mean	(1.03, 8.15)
P-value	0.0139

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	23
Mean (SD)	81.16 (19.66)
Week 4 (MMRM)	
n	23
LS mean (SE)	89.86 (2.55)
95% CI of LS mean	(84.52, 95.19)
Absolute Change at Week 4 (MMRM)	
n	23
LS mean (SE)	8.70 (2.55)
95% CI of LS mean	(3.37, 14.03)
Week 8 (MMRM)	
n	23
LS mean (SE)	86.96 (4.19)
95% CI of LS mean	(78.24, 95.68)
Absolute Change at Week 8 (MMRM)	
n	23
LS mean (SE)	5.80 (4.19)
95% CI of LS mean	(-2.92, 14.52)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	23
LS mean (SE)	82.61 (3.14)
95% CI of LS mean	(76.10, 89.12)
Absolute Change at Week 12 (MMRM)	
n	23
LS mean (SE)	1.45 (3.14)
95% CI of LS mean	(-5.06, 7.96)
Week 16 (MMRM)	
n	23
LS mean (SE)	86.96 (3.98)
95% CI of LS mean	(78.69, 95.23)
Absolute Change at Week 16 (MMRM)	
n	23
LS mean (SE)	5.80 (3.98)
95% CI of LS mean	(-2.47, 14.07)
Week 24	
n	24
Mean (SD)	87.50 (19.19)
Absolute Change at Week 24	
n	23
Mean (SD)	7.25 (28.35)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	88.41 (4.41)
95% CI of LS mean	(79.20, 97.61)
Absolute Change at Week 24 (MMRM)	
n	23
LS mean (SE)	7.25 (4.41)
95% CI of LS mean	(-1.96, 16.45)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	6.52 (3.07)
95% CI of LS mean	(0.07, 12.97)
P-value	0.0478

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	23
Mean (SD)	88.89 (17.41)
Week 4 (MMRM)	
n	23
LS mean (SE)	87.44 (3.04)
95% CI of LS mean	(81.10, 93.78)
Absolute Change at Week 4 (MMRM)	
n	23
LS mean (SE)	-1.45 (3.04)
95% CI of LS mean	(-7.79, 4.89)
Week 8 (MMRM)	
n	23
LS mean (SE)	86.47 (4.68)
95% CI of LS mean	(76.74, 96.21)
Absolute Change at Week 8 (MMRM)	
n	23
LS mean (SE)	-2.42 (4.68)
95% CI of LS mean	(-12.15, 7.32)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	23
LS mean (SE)	84.54 (4.18)
95% CI of LS mean	(75.85, 93.23)
Absolute Change at Week 12 (MMRM)	
n	23
LS mean (SE)	-4.35 (4.18)
95% CI of LS mean	(-13.04, 4.34)
Week 16 (MMRM)	
n	23
LS mean (SE)	85.02 (4.86)
95% CI of LS mean	(74.91, 95.14)
Absolute Change at Week 16 (MMRM)	
n	23
LS mean (SE)	-3.86 (4.86)
95% CI of LS mean	(-13.98, 6.25)
Week 24	
n	24
Mean (SD)	91.67 (17.10)
Absolute Change at Week 24	
n	23
Mean (SD)	2.42 (13.38)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	91.30 (2.79)
95% CI of LS mean	(85.42, 97.18)
Absolute Change at Week 24 (MMRM)	
n	23
LS mean (SE)	2.42 (2.79)
95% CI of LS mean	(-3.46, 8.29)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	-0.72 (3.46)
95% CI of LS mean	(-7.96, 6.51)
P-value	0.8363

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	23
Mean (SD)	84.42 (10.07)
Week 4 (MMRM)	
n	23
LS mean (SE)	83.70 (2.56)
95% CI of LS mean	(78.34, 89.06)
Absolute Change at Week 4 (MMRM)	
n	23
LS mean (SE)	-0.72 (2.56)
95% CI of LS mean	(-6.09, 4.64)
Week 8 (MMRM)	
n	23
LS mean (SE)	83.15 (2.53)
95% CI of LS mean	(77.81, 88.50)
Absolute Change at Week 8 (MMRM)	
n	23
LS mean (SE)	-1.27 (2.53)
95% CI of LS mean	(-6.61, 4.08)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	23
LS mean (SE)	84.06 (3.37)
95% CI of LS mean	(76.99, 91.12)
Absolute Change at Week 12 (MMRM)	
n	23
LS mean (SE)	-0.36 (3.37)
95% CI of LS mean	(-7.43, 6.70)
Week 16 (MMRM)	
n	23
LS mean (SE)	81.16 (3.14)
95% CI of LS mean	(74.63, 87.68)
Absolute Change at Week 16 (MMRM)	
n	23
LS mean (SE)	-3.26 (3.14)
95% CI of LS mean	(-9.79, 3.26)
Week 24	
n	24
Mean (SD)	82.81 (14.76)
Absolute Change at Week 24	
n	23
Mean (SD)	-1.27 (9.93)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	83.15 (2.10)
95% CI of LS mean	(78.79, 87.51)
Absolute Change at Week 24 (MMRM)	
n	23
LS mean (SE)	-1.27 (2.10)
95% CI of LS mean	(-5.63, 3.09)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	-2.26 (2.40)
95% CI of LS mean	(-7.26, 2.73)
P-value	0.3559

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	23
Mean (SD)	89.37 (13.29)
Week 4 (MMRM)	
n	23
LS mean (SE)	87.92 (1.88)
95% CI of LS mean	(84.01, 91.84)
Absolute Change at Week 4 (MMRM)	
n	23
LS mean (SE)	-1.45 (1.88)
95% CI of LS mean	(-5.36, 2.47)
Week 8 (MMRM)	
n	23
LS mean (SE)	89.37 (2.78)
95% CI of LS mean	(83.61, 95.13)
Absolute Change at Week 8 (MMRM)	
n	23
LS mean (SE)	0.00 (2.78)
95% CI of LS mean	(-5.76, 5.76)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	23
LS mean (SE)	87.92 (3.73)
95% CI of LS mean	(80.18, 95.66)
Absolute Change at Week 12 (MMRM)	
n	23
LS mean (SE)	-1.45 (3.73)
95% CI of LS mean	(-9.19, 6.29)
Week 16 (MMRM)	
n	23
LS mean (SE)	87.44 (2.76)
95% CI of LS mean	(81.72, 93.16)
Absolute Change at Week 16 (MMRM)	
n	23
LS mean (SE)	-1.93 (2.76)
95% CI of LS mean	(-7.66, 3.79)
Week 24	
n	24
Mean (SD)	92.13 (11.80)
Absolute Change at Week 24	
n	23
Mean (SD)	2.42 (9.45)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	91.79 (1.76)
95% CI of LS mean	(88.12, 95.45)
Absolute Change at Week 24 (MMRM)	
n	23
LS mean (SE)	2.42 (1.76)
95% CI of LS mean	(-1.25, 6.08)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	0.24 (1.96)
95% CI of LS mean	(-3.84, 4.32)
P-value	0.9033

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Social

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	23
Mean (SD)	71.01 (15.66)
Week 4 (MMRM)	
n	23
LS mean (SE)	70.81 (2.71)
95% CI of LS mean	(65.17, 76.44)
Absolute Change at Week 4 (MMRM)	
n	23
LS mean (SE)	-0.21 (2.71)
95% CI of LS mean	(-5.84, 5.43)
Week 8 (MMRM)	
n	23
LS mean (SE)	70.39 (3.30)
95% CI of LS mean	(63.54, 77.25)
Absolute Change at Week 8 (MMRM)	
n	23
LS mean (SE)	-0.62 (3.30)
95% CI of LS mean	(-7.48, 6.23)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Social

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	23
LS mean (SE)	71.84 (2.86)
95% CI of LS mean	(65.90, 77.79)
Absolute Change at Week 12 (MMRM)	
n	23
LS mean (SE)	0.83 (2.86)
95% CI of LS mean	(-5.12, 6.78)
Week 16 (MMRM)	
n	23
LS mean (SE)	73.08 (3.10)
95% CI of LS mean	(66.66, 79.51)
Absolute Change at Week 16 (MMRM)	
n	23
LS mean (SE)	2.07 (3.10)
95% CI of LS mean	(-4.36, 8.50)
Week 24	
n	24
Mean (SD)	75.89 (15.29)
Absolute Change at Week 24	
n	23
Mean (SD)	5.07 (17.73)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Social

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	76.09 (3.12)
95% CI of LS mean	(69.61, 82.57)
Absolute Change at Week 24 (MMRM)	
n	23
LS mean (SE)	5.07 (3.12)
95% CI of LS mean	(-1.41, 11.55)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	3.57 (2.85)
95% CI of LS mean	(-2.35, 9.50)
P-value	0.2241

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	23
Mean (SD)	78.99 (19.53)
Week 4 (MMRM)	
n	23
LS mean (SE)	81.16 (3.71)
95% CI of LS mean	(73.47, 88.85)
Absolute Change at Week 4 (MMRM)	
n	23
LS mean (SE)	2.17 (3.71)
95% CI of LS mean	(-5.52, 9.87)
Week 8 (MMRM)	
n	23
LS mean (SE)	84.06 (2.63)
95% CI of LS mean	(78.59, 89.53)
Absolute Change at Week 8 (MMRM)	
n	23
LS mean (SE)	5.07 (2.63)
95% CI of LS mean	(-0.40, 10.55)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	23
LS mean (SE)	84.54 (2.55)
95% CI of LS mean	(79.25, 89.84)
Absolute Change at Week 12 (MMRM)	
n	23
LS mean (SE)	5.56 (2.55)
95% CI of LS mean	(0.26, 10.85)
Week 16 (MMRM)	
n	23
LS mean (SE)	79.23 (4.68)
95% CI of LS mean	(69.52, 88.94)
Absolute Change at Week 16 (MMRM)	
n	23
LS mean (SE)	0.24 (4.68)
95% CI of LS mean	(-9.47, 9.95)
Week 24	
n	24
Mean (SD)	84.26 (20.18)
Absolute Change at Week 24	
n	23
Mean (SD)	5.56 (15.08)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	84.54 (3.03)
95% CI of LS mean	(78.24, 90.84)
Absolute Change at Week 24 (MMRM)	
n	23
LS mean (SE)	5.56 (3.03)
95% CI of LS mean	(-0.74, 11.85)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	2.90 (2.81)
95% CI of LS mean	(-2.94, 8.73)
P-value	0.3136

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	82.41 (25.57)
Week 4 (MMRM)	
n	24
LS mean (SE)	80.56 (2.81)
95% CI of LS mean	(74.74, 86.37)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	-1.85 (2.81)
95% CI of LS mean	(-7.67, 3.96)
Week 8 (MMRM)	
n	24
LS mean (SE)	85.19 (2.21)
95% CI of LS mean	(80.61, 89.76)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	2.78 (2.21)
95% CI of LS mean	(-1.80, 7.35)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	84.26 (2.88)
95% CI of LS mean	(78.29, 90.23)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	1.85 (2.88)
95% CI of LS mean	(-4.12, 7.82)
Week 16 (MMRM)	
n	24
LS mean (SE)	86.11 (2.43)
95% CI of LS mean	(81.08, 91.14)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	3.70 (2.43)
95% CI of LS mean	(-1.33, 8.74)
Week 24	
n	24
Mean (SD)	86.11 (24.79)
Absolute Change at Week 24	
n	24
Mean (SD)	3.70 (7.08)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	86.11 (1.43)
95% CI of LS mean	(83.15, 89.07)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	3.70 (1.43)
95% CI of LS mean	(0.75, 6.66)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	3.70 (1.66)
95% CI of LS mean	(0.27, 7.14)
P-value	0.0357

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	81.48 (17.54)
Week 4 (MMRM)	
n	24
LS mean (SE)	82.41 (1.98)
95% CI of LS mean	(78.31, 86.51)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	0.93 (1.98)
95% CI of LS mean	(-3.18, 5.03)
Week 8 (MMRM)	
n	24
LS mean (SE)	82.87 (3.00)
95% CI of LS mean	(76.66, 89.08)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	1.39 (3.00)
95% CI of LS mean	(-4.82, 7.60)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	82.41 (2.55)
95% CI of LS mean	(77.12, 87.70)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	0.93 (2.55)
95% CI of LS mean	(-4.37, 6.22)
Week 16 (MMRM)	
n	24
LS mean (SE)	85.19 (2.12)
95% CI of LS mean	(80.79, 89.58)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	3.70 (2.12)
95% CI of LS mean	(-0.69, 8.10)
Week 24	
n	24
Mean (SD)	81.48 (20.11)
Absolute Change at Week 24	
n	24
Mean (SD)	0.00 (15.01)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	81.48 (3.02)
95% CI of LS mean	(75.24, 87.73)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	0.00 (3.02)
95% CI of LS mean	(-6.25, 6.25)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	1.85 (2.24)
95% CI of LS mean	(-2.79, 6.50)
P-value	0.4179

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	86.11 (23.91)
Week 4 (MMRM)	
n	24
LS mean (SE)	84.72 (3.27)
95% CI of LS mean	(77.93, 91.51)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	-1.39 (3.27)
95% CI of LS mean	(-8.18, 5.40)
Week 8 (MMRM)	
n	24
LS mean (SE)	88.19 (2.91)
95% CI of LS mean	(82.16, 94.22)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	2.08 (2.91)
95% CI of LS mean	(-3.95, 8.11)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	84.03 (3.61)
95% CI of LS mean	(76.53, 91.52)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	-2.08 (3.61)
95% CI of LS mean	(-9.58, 5.41)
Week 16 (MMRM)	
n	24
LS mean (SE)	86.11 (3.31)
95% CI of LS mean	(79.26, 92.97)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	0.00 (3.31)
95% CI of LS mean	(-6.86, 6.86)
Week 24	
n	24
Mean (SD)	85.42 (27.06)
Absolute Change at Week 24	
n	24
Mean (SD)	-0.69 (15.91)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	85.42 (3.27)
95% CI of LS mean	(78.64, 92.19)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	-0.69 (3.27)
95% CI of LS mean	(-7.47, 6.08)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	-0.35 (3.03)
95% CI of LS mean	(-6.63, 5.94)
P-value	0.9099

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	89.72 (9.00)
Week 4 (MMRM)	
n	24
LS mean (SE)	89.72 (2.29)
95% CI of LS mean	(84.98, 94.47)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	0.00 (2.29)
95% CI of LS mean	(-4.75, 4.75)
Week 8 (MMRM)	
n	24
LS mean (SE)	90.00 (1.93)
95% CI of LS mean	(85.97, 94.03)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	0.28 (1.93)
95% CI of LS mean	(-3.75, 4.31)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	91.67 (1.53)
95% CI of LS mean	(88.50, 94.84)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	1.94 (1.53)
95% CI of LS mean	(-1.23, 5.11)
Week 16 (MMRM)	
n	24
LS mean (SE)	91.39 (1.89)
95% CI of LS mean	(87.48, 95.30)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	1.67 (1.89)
95% CI of LS mean	(-2.24, 5.57)
Week 24	
n	24
Mean (SD)	87.78 (12.69)
Absolute Change at Week 24	
n	24
Mean (SD)	-1.94 (11.03)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	87.78 (2.29)
95% CI of LS mean	(83.02, 92.53)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	-1.94 (2.29)
95% CI of LS mean	(-6.70, 2.81)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	-0.14 (1.84)
95% CI of LS mean	(-3.96, 3.69)
P-value	0.9406

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	87.04 (14.53)
Week 4 (MMRM)	
n	24
LS mean (SE)	80.56 (3.15)
95% CI of LS mean	(74.03, 87.08)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	-6.48 (3.15)
95% CI of LS mean	(-13.01, 0.04)
Week 8 (MMRM)	
n	24
LS mean (SE)	82.41 (2.93)
95% CI of LS mean	(76.32, 88.49)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	-4.63 (2.93)
95% CI of LS mean	(-10.71, 1.46)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	86.57 (1.85)
95% CI of LS mean	(82.73, 90.42)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	-0.46 (1.85)
95% CI of LS mean	(-4.31, 3.38)
Week 16 (MMRM)	
n	24
LS mean (SE)	86.57 (2.41)
95% CI of LS mean	(81.59, 91.55)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	-0.46 (2.41)
95% CI of LS mean	(-5.44, 4.52)
Week 24	
n	24
Mean (SD)	88.43 (14.08)
Absolute Change at Week 24	
n	24
Mean (SD)	1.39 (11.50)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	88.43 (2.14)
95% CI of LS mean	(84.01, 92.85)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	1.39 (2.14)
95% CI of LS mean	(-3.03, 5.81)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	0.46 (1.52)
95% CI of LS mean	(-2.68, 3.61)
P-value	0.7633

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	94.62 (8.01)
Week 4 (MMRM)	
n	24
LS mean (SE)	90.80 (2.55)
95% CI of LS mean	(85.53, 96.07)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	-3.82 (2.55)
95% CI of LS mean	(-9.09, 1.45)
Week 8 (MMRM)	
n	24
LS mean (SE)	89.06 (2.75)
95% CI of LS mean	(83.37, 94.76)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	-5.56 (2.75)
95% CI of LS mean	(-11.25, 0.14)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	95.31 (1.38)
95% CI of LS mean	(92.40, 98.22)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	0.69 (1.38)
95% CI of LS mean	(-2.22, 3.61)
Week 16 (MMRM)	
n	24
LS mean (SE)	93.40 (2.21)
95% CI of LS mean	(88.76, 98.04)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	-1.22 (2.21)
95% CI of LS mean	(-5.85, 3.42)
Week 24	
n	24
Mean (SD)	93.40 (14.53)
Absolute Change at Week 24	
n	24
Mean (SD)	-1.22 (10.32)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	93.40 (2.17)
95% CI of LS mean	(88.87, 97.93)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	-1.22 (2.17)
95% CI of LS mean	(-5.75, 3.32)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	-1.22 (1.72)
95% CI of LS mean	(-4.90, 2.47)
P-value	0.4916

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	85.42 (14.17)
Week 4 (MMRM)	
n	24
LS mean (SE)	81.60 (3.44)
95% CI of LS mean	(74.45, 88.75)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	-3.82 (3.44)
95% CI of LS mean	(-10.97, 3.33)
Week 8 (MMRM)	
n	24
LS mean (SE)	80.90 (3.18)
95% CI of LS mean	(74.32, 87.48)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	-4.51 (3.18)
95% CI of LS mean	(-11.09, 2.07)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	82.41 (2.59)
95% CI of LS mean	(77.01, 87.80)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	-3.01 (2.59)
95% CI of LS mean	(-8.40, 2.38)
Week 16 (MMRM)	
n	24
LS mean (SE)	87.85 (2.48)
95% CI of LS mean	(82.63, 93.06)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	2.43 (2.48)
95% CI of LS mean	(-2.79, 7.65)
Week 24	
n	24
Mean (SD)	84.72 (18.82)
Absolute Change at Week 24	
n	24
Mean (SD)	-0.69 (17.19)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	84.72 (3.40)
95% CI of LS mean	(77.69, 91.76)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	-0.69 (3.40)
95% CI of LS mean	(-7.73, 6.34)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	0.87 (2.63)
95% CI of LS mean	(-4.61, 6.34)
P-value	0.7447

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	67.13 (23.74)
Week 4 (MMRM)	
n	24
LS mean (SE)	71.76 (3.29)
95% CI of LS mean	(64.90, 78.61)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	4.63 (3.29)
95% CI of LS mean	(-2.22, 11.48)
Week 8 (MMRM)	
n	24
LS mean (SE)	75.00 (4.08)
95% CI of LS mean	(66.47, 83.53)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	7.87 (4.08)
95% CI of LS mean	(-0.66, 16.40)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	71.30 (3.63)
95% CI of LS mean	(63.76, 78.83)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	4.17 (3.63)
95% CI of LS mean	(-3.37, 11.70)
Week 16 (MMRM)	
n	24
LS mean (SE)	74.54 (2.81)
95% CI of LS mean	(68.70, 80.37)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	7.41 (2.81)
95% CI of LS mean	(1.57, 13.24)
Week 24	
n	24
Mean (SD)	73.15 (24.72)
Absolute Change at Week 24	
n	24
Mean (SD)	6.02 (18.24)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	73.15 (3.56)
95% CI of LS mean	(65.79, 80.51)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	6.02 (3.56)
95% CI of LS mean	(-1.34, 13.38)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	6.71 (2.91)
95% CI of LS mean	(0.69, 12.74)
P-value	0.0306

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	79.44 (12.73)
Week 4 (MMRM)	
n	24
LS mean (SE)	80.00 (2.61)
95% CI of LS mean	(74.58, 85.42)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	0.56 (2.61)
95% CI of LS mean	(-4.86, 5.97)
Week 8 (MMRM)	
n	24
LS mean (SE)	80.00 (1.94)
95% CI of LS mean	(75.99, 84.01)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	0.56 (1.94)
95% CI of LS mean	(-3.45, 4.56)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	80.28 (2.25)
95% CI of LS mean	(75.61, 84.95)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	0.83 (2.25)
95% CI of LS mean	(-3.83, 5.50)
Week 16 (MMRM)	
n	24
LS mean (SE)	81.39 (2.82)
95% CI of LS mean	(75.54, 87.24)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	1.94 (2.82)
95% CI of LS mean	(-3.91, 7.80)
Week 24	
n	24
Mean (SD)	78.06 (15.41)
Absolute Change at Week 24	
n	24
Mean (SD)	-1.39 (12.27)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	78.06 (2.46)
95% CI of LS mean	(72.96, 83.15)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	-1.39 (2.46)
95% CI of LS mean	(-6.48, 3.71)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	0.28 (2.18)
95% CI of LS mean	(-4.24, 4.80)
P-value	0.8998

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	63.89 (35.33)
Week 4 (MMRM)	
n	24
LS mean (SE)	70.83 (4.31)
95% CI of LS mean	(61.90, 79.77)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	6.94 (4.31)
95% CI of LS mean	(-1.99, 15.88)
Week 8 (MMRM)	
n	24
LS mean (SE)	70.83 (4.37)
95% CI of LS mean	(61.78, 79.89)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	6.94 (4.37)
95% CI of LS mean	(-2.11, 16.00)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	69.44 (5.41)
95% CI of LS mean	(58.23, 80.66)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	5.56 (5.41)
95% CI of LS mean	(-5.66, 16.77)
Week 16 (MMRM)	
n	24
LS mean (SE)	66.67 (5.71)
95% CI of LS mean	(54.80, 78.54)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	2.78 (5.71)
95% CI of LS mean	(-9.09, 14.65)
Week 24	
n	24
Mean (SD)	69.44 (40.43)
Absolute Change at Week 24	
n	24
Mean (SD)	5.56 (21.23)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	69.44 (4.47)
95% CI of LS mean	(60.17, 78.72)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	5.56 (4.47)
95% CI of LS mean	(-3.72, 14.83)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	4.17 (4.40)
95% CI of LS mean	(-4.95, 13.28)
P-value	0.3535

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.13
Study VX21-121-105: Summary of Pulmonary Exacerbations through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Total number of days (years) of the PEx analysis period	4040 (12.0)
Pulmonary exacerbations	
Number of subjects with events, n (%)	2 (8.33)
Total number of events	2
Observed event rate per year	0.17
Pulmonary exacerbations requiring hospitalization	
Number of subjects with events, n (%)	0
Total number of events	0
Observed event rate per year	0
Pulmonary exacerbations requiring IV antibiotic therapy	
Number of subjects with events, n (%)	0
Total number of events	0
Observed event rate per year	0
Pulmonary exacerbations requiring hospitalization or IV antibiotic therapy	
Number of subjects with events, n (%)	0
Total number of events	0
Observed event rate per year	0

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 1.2.1.14.1
Study VX21-121-105: Time-to-First Pulmonary Exacerbation through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Any Pulmonary Exacerbation	
Overall	
Subjects with Events	2 (8.33)
Subjects Censored	22 (91.67)
Event-free time (weeks)	
75 percent subjects	-
50 percent subjects (Median)	-
25 percent subjects	-

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.1.15.1
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization	
Overall	
Subjects with Events	0
Subjects Censored	24 (100.00)
Event-free time (weeks)	
75 percent subjects	-
50 percent subjects (Median)	-
25 percent subjects	-

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation requiring hospitalization during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.1.16.1
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics	
Overall	
Subjects with Events	0
Subjects Censored	24 (100.00)
Event-free time (weeks)	
75 percent subjects	-
50 percent subjects (Median)	-
25 percent subjects	-

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation requiring IV antibiotics during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.1.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.7089
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effects and baseline $ppFEV_1$ as covariate.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA
	N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline ppFEV$_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline ppFEV$_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	104.07 (17.53)
Week 24	
n	10
Mean (SD)	102.94 (16.03)
Absolute Change at Week 24	
n	10
Mean (SD)	-1.83 (6.29)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	-2.06 (1.37)
95% CI of LS mean	(-5.32, 1.21)
P-value	0.1793

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline ppFEV$_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	85.95 (21.22)
Week 24	
n	10
Mean (SD)	91.51 (18.18)
Absolute Change at Week 24	
n	10
Mean (SD)	2.60 (7.50)
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	4.40 (3.29)
95% CI of LS mean	(-2.94, 11.75)
P-value	0.2107

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline ppFEV$_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 24 by Subgroups for F/MF
Full Analysis Set
LCI$_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline ppFEV$_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 24 by Subgroups for F/MF
Full Analysis Set
LCI$_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline ppFEV$_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.2.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.4544
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effects and baseline BMI as covariate.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	18.17 (2.39)
Week 24	
n	11
Mean (SD)	18.40 (2.56)
Absolute Change at Week 24	
n	11
Mean (SD)	0.23 (0.42)
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	0.23 (0.13)
95% CI of LS mean	(-0.07, 0.53)
P-value	0.1207

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	15.94 (1.27)
Week 24	
n	13
Mean (SD)	16.04 (1.72)
Absolute Change at Week 24	
n	13
Mean (SD)	0.09 (0.78)
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	0.09 (0.22)
95% CI of LS mean	(-0.39, 0.57)
P-value	0.6819

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.3524
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effect and baseline BMI z-score as covariate.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	0.47 (0.91)
Week 24	
n	11
Mean (SD)	0.44 (0.94)
Absolute Change at Week 24	
n	11
Mean (SD)	-0.04 (0.13)
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	-0.04 (0.04)
95% CI of LS mean	(-0.12, 0.05)
P-value	0.3910

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	-0.26 (0.84)
Week 24	
n	13
Mean (SD)	-0.39 (1.00)
Absolute Change at Week 24	
n	13
Mean (SD)	-0.13 (0.42)
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	-0.13 (0.12)
95% CI of LS mean	(-0.39, 0.12)
P-value	0.2795

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.9086
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effects and baseline sweat chloride as covariate.
- N/C: model does not converge.

Table 1.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA
	N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	48.14 (20.22)
Week 24	
n	10
Mean (SD)	39.85 (16.97)
Absolute Change at Week 24	
n	10
Mean (SD)	-10.40 (9.51)
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	-7.62 (2.48)
95% CI of LS mean	(-13.20, -2.05)
P-value	0.0127

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	12
Mean (SD)	56.67 (17.42)
Week 24	
n	12
Mean (SD)	44.17 (15.14)
Absolute Change at Week 24	
n	12
Mean (SD)	-12.50 (11.35)
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	-13.27 (3.36)
95% CI of LS mean	(-20.69, -5.85)
P-value	0.0024

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.2.4.2.1
Study VX21-121-105: Subgroup Factor Test for
Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.8130
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Chi-square test.

Table 1.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 1.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 1.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Non-missing value at Week 24, N1	10
Number of subjects with missing value at Week 24	1
SwCl <60 mmol/L at Week 24, n (%)	8 (72.73)
95% CI for the proportion	(39.03, 93.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 1.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Non-missing value at Week 24, N1	12
Number of subjects with missing value at Week 24	1
SwCl <60 mmol/L at Week 24, n (%)	10 (76.92)
95% CI for the proportion	(46.19, 94.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 1.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 1.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 1.2.2.4.3.1
Study VX21-121-105: Subgroup Factor Test for
Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Chi-square test.

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Table 1.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 1.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 1.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 1.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 1.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 1.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 1.2.2.5.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.6517
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effects and baseline weight as covariate.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	33.31 (4.69)
Week 24	
n	11
Mean (SD)	35.11 (5.26)
Absolute Change at Week 24	
n	11
Mean (SD)	1.80 (0.87)
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	1.80 (0.26)
95% CI of LS mean	(1.21, 2.40)
P-value	0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	28.55 (5.48)
Week 24	
n	13
Mean (SD)	29.99 (6.11)
Absolute Change at Week 24	
n	13
Mean (SD)	1.45 (1.60)
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	1.45 (0.45)
95% CI of LS mean	(0.46, 2.43)
P-value	0.0079

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

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Table 1.2.2.6.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.6578
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effects and baseline weight z-score as covariate.
- N/C: model does not converge.

Table 1.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA
	N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	0.16 (0.80)
Week 24	
n	11
Mean (SD)	0.15 (0.85)
Absolute Change at Week 24	
n	11
Mean (SD)	-0.01 (0.11)
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	-0.01 (0.03)
95% CI of LS mean	(-0.09, 0.07)
P-value	0.7696

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	-0.14 (0.94)
Week 24	
n	13
Mean (SD)	-0.20 (1.05)
Absolute Change at Week 24	
n	13
Mean (SD)	-0.06 (0.29)
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	-0.06 (0.08)
95% CI of LS mean	(-0.24, 0.12)
P-value	0.5004

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

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Table 1.2.2.7.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.7490
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effects and baseline height as covariate.
- N/C: model does not converge.

Table 1.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	135.48 (7.56)
Week 24	
n	11
Mean (SD)	138.21 (7.55)
Absolute Change at Week 24	
n	11
Mean (SD)	2.73 (0.78)
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	2.73 (0.25)
95% CI of LS mean	(2.17, 3.28)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	133.31 (10.78)
Week 24	
n	13
Mean (SD)	136.22 (11.06)
Absolute Change at Week 24	
n	13
Mean (SD)	2.92 (1.16)
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	2.92 (0.32)
95% CI of LS mean	(2.22, 3.62)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.8.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.3427
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effect and baseline height z-score as covariate.
- N/C: model does not converge.

Table 1.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	-0.32 (0.85)
Week 24	
n	11
Mean (SD)	-0.28 (0.86)
Absolute Change at Week 24	
n	11
Mean (SD)	0.04 (0.14)
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	0.04 (0.04)
95% CI of LS mean	(-0.05, 0.14)
P-value	0.3514

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	0.14 (0.98)
Week 24	
n	13
Mean (SD)	0.17 (0.98)
Absolute Change at Week 24	
n	13
Mean (SD)	0.03 (0.16)
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	0.03 (0.04)
95% CI of LS mean	(-0.07, 0.12)
P-value	0.5641

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

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Table 1.2.2.9.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.4223
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline $LCI_{2.5}$ as covariate.
- N/C: model does not converge.

Table 1.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 1.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 1.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	10
Mean (SD)	6.94 (0.98)
Week 24	
n	8
Mean (SD)	6.45 (0.67)
Absolute Change at Week 24	
n	8
Mean (SD)	-0.21 (0.64)
Absolute Change through Week 24 (MMRM)	
n	8
LS mean (SE)	-0.17 (0.12)
95% CI of LS mean	(-0.45, 0.11)
P-value	0.1976

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 1.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	11
Mean (SD)	6.91 (1.18)
Week 24	
n	9
Mean (SD)	6.50 (0.58)
Absolute Change at Week 24	
n	8
Mean (SD)	-0.26 (0.63)
Absolute Change through Week 24 (MMRM)	
n	8
LS mean (SE)	0.24 (0.24)
95% CI of LS mean	(-0.37, 0.86)
P-value	0.3496

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 1.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 1.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.9564
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Respiratory domain score as covariate.
- N/C: model does not converge.

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Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	87.88 (6.83)
Week 4 (MMRM)	
n	11
LS mean (SE)	89.39 (3.13)
95% CI of LS mean	(82.42, 96.36)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	1.52 (3.13)
95% CI of LS mean	(-5.46, 8.49)
Week 8 (MMRM)	
n	11
LS mean (SE)	90.91 (2.79)
95% CI of LS mean	(84.69, 97.13)
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	3.03 (2.79)
95% CI of LS mean	(-3.19, 9.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Week 12 (MMRM)	
n	11
LS mean (SE)	91.67 (1.92)
95% CI of LS mean	(87.39, 95.94)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	3.79 (1.92)
95% CI of LS mean	(-0.49, 8.06)
Week 16 (MMRM)	
n	11
LS mean (SE)	89.39 (3.16)
95% CI of LS mean	(82.27, 96.52)
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	1.52 (3.16)
95% CI of LS mean	(-5.61, 8.64)
Week 24	
n	11
Mean (SD)	91.67 (8.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 24	
n	11
Mean (SD)	3.79 (10.78)
Week 24 (MMRM)	
n	11
LS mean (SE)	91.67 (2.77)
95% CI of LS mean	(85.42, 97.91)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	3.79 (2.77)
95% CI of LS mean	(-2.45, 10.03)
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	2.65 (2.57)
95% CI of LS mean	(-3.19, 8.49)
P-value	0.3301

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	12
Mean (SD)	91.67 (8.70)
Week 4 (MMRM)	
n	12
LS mean (SE)	90.97 (2.18)
95% CI of LS mean	(86.16, 95.78)
Absolute Change at Week 4 (MMRM)	
n	12
LS mean (SE)	-0.69 (2.18)
95% CI of LS mean	(-5.51, 4.12)
Week 8 (MMRM)	
n	12
LS mean (SE)	88.19 (4.03)
95% CI of LS mean	(79.29, 97.09)
Absolute Change at Week 8 (MMRM)	
n	12
LS mean (SE)	-3.47 (4.03)
95% CI of LS mean	(-12.37, 5.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Week 12 (MMRM)	
n	12
LS mean (SE)	91.67 (3.27)
95% CI of LS mean	(84.39, 98.95)
Absolute Change at Week 12 (MMRM)	
n	12
LS mean (SE)	0.00 (3.27)
95% CI of LS mean	(-7.28, 7.28)
Week 16 (MMRM)	
n	12
LS mean (SE)	93.75 (2.15)
95% CI of LS mean	(89.00, 98.50)
Absolute Change at Week 16 (MMRM)	
n	12
LS mean (SE)	2.08 (2.15)
95% CI of LS mean	(-2.67, 6.83)
Week 24	
n	13
Mean (SD)	87.18 (12.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 24	
n	12
Mean (SD)	-4.86 (9.03)
Week 24 (MMRM)	
n	13
LS mean (SE)	86.81 (2.83)
95% CI of LS mean	(80.52, 93.09)
Absolute Change at Week 24 (MMRM)	
n	12
LS mean (SE)	-4.86 (2.83)
95% CI of LS mean	(-11.15, 1.43)
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	-1.39 (1.63)
95% CI of LS mean	(-5.02, 2.24)
P-value	0.4145

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.2.10.2.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.5972
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Respiratory domain score as covariate.
- N/C: model does not converge.

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Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	90.91 (9.71)
Week 4 (MMRM)	
n	11
LS mean (SE)	83.33 (4.66)
95% CI of LS mean	(72.85, 93.82)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	-7.58 (4.66)
95% CI of LS mean	(-18.06, 2.91)
Week 8 (MMRM)	
n	11
LS mean (SE)	88.89 (5.73)
95% CI of LS mean	(76.09, 101.68)
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	-2.02 (5.73)
95% CI of LS mean	(-14.82, 10.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Week 12 (MMRM)	
n	11
LS mean (SE)	93.43 (2.28)
95% CI of LS mean	(87.73, 99.14)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	2.53 (2.28)
95% CI of LS mean	(-3.18, 8.23)
Week 16 (MMRM)	
n	11
LS mean (SE)	88.38 (4.79)
95% CI of LS mean	(77.38, 99.39)
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	-2.53 (4.79)
95% CI of LS mean	(-13.53, 8.48)
Week 24	
n	11
Mean (SD)	88.38 (13.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 24	
n	11
Mean (SD)	-2.53 (15.19)
Week 24 (MMRM)	
n	11
LS mean (SE)	88.38 (4.81)
95% CI of LS mean	(77.43, 99.34)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	-2.53 (4.81)
95% CI of LS mean	(-13.48, 8.43)
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	-2.53 (4.11)
95% CI of LS mean	(-12.13, 7.08)
P-value	0.5572

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	92.22 (9.48)
Week 4 (MMRM)	
n	13
LS mean (SE)	83.76 (4.53)
95% CI of LS mean	(73.85, 93.67)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	-8.46 (4.53)
95% CI of LS mean	(-18.37, 1.44)
Week 8 (MMRM)	
n	13
LS mean (SE)	85.04 (4.80)
95% CI of LS mean	(74.59, 95.49)
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	-7.18 (4.80)
95% CI of LS mean	(-17.63, 3.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Week 12 (MMRM)	
n	13
LS mean (SE)	92.74 (2.15)
95% CI of LS mean	(88.03, 97.44)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	0.51 (2.15)
95% CI of LS mean	(-4.19, 5.22)
Week 16 (MMRM)	
n	13
LS mean (SE)	94.87 (2.75)
95% CI of LS mean	(88.74, 101.00)
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	2.65 (2.75)
95% CI of LS mean	(-3.48, 8.78)
Week 24	
n	13
Mean (SD)	88.46 (14.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 24	
n	13
Mean (SD)	-3.76 (16.81)
Week 24 (MMRM)	
n	13
LS mean (SE)	88.46 (4.07)
95% CI of LS mean	(79.59, 97.33)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	-3.76 (4.07)
95% CI of LS mean	(-12.63, 5.11)
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	-0.56 (1.84)
95% CI of LS mean	(-4.59, 3.48)
P-value	0.7678

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-105\t-qs-mmrm-abs-cfqr-rd-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 8:29

Table 1.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Body

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.4469
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Body domain score as covariate.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-105\t-qs-mmrm-abs-cfqr-nonrd-ch-24wks-sub-test-b1-fmf.sas Creation: 06FEB2025 8:17

Table 1.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Digestion

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.1011
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Digestion domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Eat

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.2829
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Eat domain score as covariate.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-105\t-qs-mmrm-abs-cfqr-nonrd-ch-24wks-sub-test-b1-fmf.sas Creation: 06FEB2025 8:17

Table 1.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Emotion

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.2133
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Emotion domain score as covariate.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-105\t-qs-mmrm-abs-cfqr-nonrd-ch-24wks-sub-test-b1-fmf.sas Creation: 06FEB2025 8:17

Table 1.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Physical

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.1715
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Physical domain score as covariate.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-105\t-qs-mmrm-abs-cfqr-nonrd-ch-24wks-sub-test-b1-fmf.sas Creation: 06FEB2025 8:17

Table 1.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Social

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.3944
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Social domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Treatment Burden

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.7733
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Treatment Burden domain score as covariate.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-105\t-qs-mmrm-abs-cfqr-nonrd-ch-24wks-sub-test-b1-fmf.sas Creation: 06FEB2025 8:17

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	85.86 (21.14)
Week 4 (MMRM)	
n	11
LS mean (SE)	90.91 (8.20)
95% CI of LS mean	(56.07, 125.75)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	5.05 (8.20)
95% CI of LS mean	(-29.79, 39.89)
Week 8 (MMRM)	
n	11
LS mean (SE)	93.94 (5.47)
95% CI of LS mean	(24.50, 163.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	8.08 (5.47)
95% CI of LS mean	(-61.36, 77.52)
Week 12 (MMRM)	
n	11
LS mean (SE)	91.92 (8.00)
95% CI of LS mean	(26.07, 157.77)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	6.06 (8.00)
95% CI of LS mean	(-59.79, 71.91)
Week 16 (MMRM)	
n	11
LS mean (SE)	92.93 (6.68)
95% CI of LS mean	(8.03, 177.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	7.07 (6.68)
95% CI of LS mean	(-77.83, 91.97)
Week 24	
n	11
Mean (SD)	94.95 (9.11)
Absolute Change at Week 24	
n	11
Mean (SD)	9.09 (18.47)
Week 24 (MMRM)	
n	11
LS mean (SE)	94.95 (5.55)
95% CI of LS mean	(24.39, 165.51)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	9.09 (5.55)
95% CI of LS mean	(-61.47, 79.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	8.08 (6.01)
95% CI of LS mean	(-68.32, 84.49)
P-value	0.4073

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	12
Mean (SD)	95.37 (8.81)
Week 4 (MMRM)	
n	12
LS mean (SE)	91.67 (4.22)
95% CI of LS mean	(82.32, 101.02)
Absolute Change at Week 4 (MMRM)	
n	12
LS mean (SE)	-3.70 (4.22)
95% CI of LS mean	(-13.05, 5.65)
Week 8 (MMRM)	
n	12
LS mean (SE)	87.04 (4.55)
95% CI of LS mean	(77.00, 97.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	12
LS mean (SE)	-8.33 (4.55)
95% CI of LS mean	(-18.37, 1.70)
Week 12 (MMRM)	
n	12
LS mean (SE)	88.89 (3.47)
95% CI of LS mean	(81.24, 96.54)
Absolute Change at Week 12 (MMRM)	
n	12
LS mean (SE)	-6.48 (3.47)
95% CI of LS mean	(-14.13, 1.17)
Week 16 (MMRM)	
n	12
LS mean (SE)	96.30 (3.90)
95% CI of LS mean	(87.57, 105.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	12
LS mean (SE)	0.93 (3.90)
95% CI of LS mean	(-7.80, 9.65)
Week 24	
n	13
Mean (SD)	94.02 (14.78)
Absolute Change at Week 24	
n	12
Mean (SD)	1.85 (11.44)
Week 24 (MMRM)	
n	13
LS mean (SE)	97.22 (3.72)
95% CI of LS mean	(88.88, 105.56)
Absolute Change at Week 24 (MMRM)	
n	12
LS mean (SE)	1.85 (3.72)
95% CI of LS mean	(-6.49, 10.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	1.39 (3.78)
95% CI of LS mean	(-7.09, 9.87)
P-value	0.7214

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	81.82 (22.92)
Week 4 (MMRM)	
n	11
LS mean (SE)	87.88 (3.06)
95% CI of LS mean	(81.02, 94.74)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	6.06 (3.06)
95% CI of LS mean	(-0.80, 12.92)
Week 8 (MMRM)	
n	11
LS mean (SE)	78.79 (7.04)
95% CI of LS mean	(62.86, 94.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	-3.03 (7.04)
95% CI of LS mean	(-18.96, 12.90)
Week 12 (MMRM)	
n	11
LS mean (SE)	78.79 (4.14)
95% CI of LS mean	(69.35, 88.22)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	-3.03 (4.14)
95% CI of LS mean	(-12.47, 6.40)
Week 16 (MMRM)	
n	11
LS mean (SE)	81.82 (6.69)
95% CI of LS mean	(66.78, 96.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	0.00 (6.69)
95% CI of LS mean	(-15.03, 15.03)
Week 24	
n	11
Mean (SD)	87.88 (16.82)
Absolute Change at Week 24	
n	11
Mean (SD)	6.06 (32.72)
Week 24 (MMRM)	
n	11
LS mean (SE)	87.88 (7.64)
95% CI of LS mean	(69.77, 105.99)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	6.06 (7.64)
95% CI of LS mean	(-12.05, 24.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	3.03 (5.68)
95% CI of LS mean	(-10.74, 16.80)
P-value	0.6123

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	12
Mean (SD)	80.56 (17.16)
Week 4 (MMRM)	
n	12
LS mean (SE)	91.67 (4.79)
95% CI of LS mean	(81.96, 101.38)
Absolute Change at Week 4 (MMRM)	
n	12
LS mean (SE)	11.11 (4.79)
95% CI of LS mean	(1.40, 20.82)
Week 8 (MMRM)	
n	12
LS mean (SE)	94.44 (4.79)
95% CI of LS mean	(84.73, 104.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	12
LS mean (SE)	13.89 (4.79)
95% CI of LS mean	(4.18, 23.60)
Week 12 (MMRM)	
n	12
LS mean (SE)	86.11 (4.79)
95% CI of LS mean	(76.40, 95.82)
Absolute Change at Week 12 (MMRM)	
n	12
LS mean (SE)	5.56 (4.79)
95% CI of LS mean	(-4.16, 15.27)
Week 16 (MMRM)	
n	12
LS mean (SE)	91.67 (4.79)
95% CI of LS mean	(81.96, 101.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	12
LS mean (SE)	11.11 (4.79)
95% CI of LS mean	(1.40, 20.82)
Week 24	
n	13
Mean (SD)	87.18 (21.68)
Absolute Change at Week 24	
n	12
Mean (SD)	8.33 (25.13)
Week 24 (MMRM)	
n	13
LS mean (SE)	88.89 (4.79)
95% CI of LS mean	(79.18, 98.60)
Absolute Change at Week 24 (MMRM)	
n	12
LS mean (SE)	8.33 (4.79)
95% CI of LS mean	(-1.38, 18.04)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	9.72 (3.88)
95% CI of LS mean	(1.65, 17.79)
P-value	0.0206

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	82.83 (22.42)
Week 4 (MMRM)	
n	11
LS mean (SE)	82.83 (5.87)
95% CI of LS mean	(69.73, 95.93)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	0.00 (5.87)
95% CI of LS mean	(-13.10, 13.10)
Week 8 (MMRM)	
n	11
LS mean (SE)	86.87 (4.90)
95% CI of LS mean	(75.62, 98.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	4.04 (4.90)
95% CI of LS mean	(-7.20, 15.29)
Week 12 (MMRM)	
n	11
LS mean (SE)	81.82 (5.66)
95% CI of LS mean	(69.11, 94.52)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	-1.01 (5.66)
95% CI of LS mean	(-13.72, 11.70)
Week 16 (MMRM)	
n	11
LS mean (SE)	76.77 (9.39)
95% CI of LS mean	(55.77, 97.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	-6.06 (9.39)
95% CI of LS mean	(-27.06, 14.94)
Week 24	
n	11
Mean (SD)	87.88 (23.02)
Absolute Change at Week 24	
n	11
Mean (SD)	5.05 (12.54)
Week 24 (MMRM)	
n	11
LS mean (SE)	87.88 (4.04)
95% CI of LS mean	(78.59, 97.16)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	5.05 (4.04)
95% CI of LS mean	(-4.23, 14.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	-0.51 (6.18)
95% CI of LS mean	(-14.44, 13.43)
P-value	0.9366

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	12
Mean (SD)	94.44 (8.86)
Week 4 (MMRM)	
n	12
LS mean (SE)	91.67 (2.25)
95% CI of LS mean	(86.54, 96.80)
Absolute Change at Week 4 (MMRM)	
n	12
LS mean (SE)	-2.78 (2.25)
95% CI of LS mean	(-7.91, 2.35)
Week 8 (MMRM)	
n	12
LS mean (SE)	86.11 (7.94)
95% CI of LS mean	(68.62, 103.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	12
LS mean (SE)	-8.33 (7.94)
95% CI of LS mean	(-25.82, 9.15)
Week 12 (MMRM)	
n	12
LS mean (SE)	87.04 (6.71)
95% CI of LS mean	(72.20, 101.87)
Absolute Change at Week 12 (MMRM)	
n	12
LS mean (SE)	-7.41 (6.71)
95% CI of LS mean	(-22.24, 7.43)
Week 16 (MMRM)	
n	12
LS mean (SE)	92.59 (5.15)
95% CI of LS mean	(81.01, 104.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	12
LS mean (SE)	-1.85 (5.15)
95% CI of LS mean	(-13.44, 9.73)
Week 24	
n	13
Mean (SD)	94.87 (9.75)
Absolute Change at Week 24	
n	12
Mean (SD)	0.00 (14.21)
Week 24 (MMRM)	
n	13
LS mean (SE)	94.44 (4.74)
95% CI of LS mean	(83.74, 105.15)
Absolute Change at Week 24 (MMRM)	
n	12
LS mean (SE)	0.00 (4.74)
95% CI of LS mean	(-10.70, 10.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	-0.93 (4.77)
95% CI of LS mean	(-11.70, 9.85)
P-value	0.8503

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	79.55 (10.11)
Week 4 (MMRM)	
n	11
LS mean (SE)	81.06 (4.10)
95% CI of LS mean	(71.47, 90.65)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	1.52 (4.10)
95% CI of LS mean	(-8.07, 11.10)
Week 8 (MMRM)	
n	11
LS mean (SE)	82.20 (3.81)
95% CI of LS mean	(72.78, 91.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	2.65 (3.81)
95% CI of LS mean	(-6.76, 12.07)
Week 12 (MMRM)	
n	11
LS mean (SE)	84.09 (5.55)
95% CI of LS mean	(71.03, 97.15)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	4.55 (5.55)
95% CI of LS mean	(-8.51, 17.60)
Week 16 (MMRM)	
n	11
LS mean (SE)	79.55 (5.38)
95% CI of LS mean	(67.40, 91.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	0.00 (5.38)
95% CI of LS mean	(-12.15, 12.15)
Week 24	
n	11
Mean (SD)	80.68 (13.85)
Absolute Change at Week 24	
n	11
Mean (SD)	1.14 (6.99)
Week 24 (MMRM)	
n	11
LS mean (SE)	80.68 (2.20)
95% CI of LS mean	(75.40, 85.96)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	1.14 (2.20)
95% CI of LS mean	(-4.15, 6.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	0.57 (3.41)
95% CI of LS mean	(-7.33, 8.47)
P-value	0.8718

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	12
Mean (SD)	88.89 (8.01)
Week 4 (MMRM)	
n	12
LS mean (SE)	86.11 (3.44)
95% CI of LS mean	(78.50, 93.72)
Absolute Change at Week 4 (MMRM)	
n	12
LS mean (SE)	-2.78 (3.44)
95% CI of LS mean	(-10.38, 4.83)
Week 8 (MMRM)	
n	12
LS mean (SE)	84.03 (3.49)
95% CI of LS mean	(76.27, 91.79)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	12
LS mean (SE)	-4.86 (3.49)
95% CI of LS mean	(-12.62, 2.90)
Week 12 (MMRM)	
n	12
LS mean (SE)	84.03 (4.28)
95% CI of LS mean	(74.51, 93.54)
Absolute Change at Week 12 (MMRM)	
n	12
LS mean (SE)	-4.86 (4.28)
95% CI of LS mean	(-14.38, 4.66)
Week 16 (MMRM)	
n	12
LS mean (SE)	82.64 (3.73)
95% CI of LS mean	(74.29, 90.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	12
LS mean (SE)	-6.25 (3.73)
95% CI of LS mean	(-14.60, 2.10)
Week 24	
n	13
Mean (SD)	84.62 (15.81)
Absolute Change at Week 24	
n	12
Mean (SD)	-3.47 (11.90)
Week 24 (MMRM)	
n	13
LS mean (SE)	85.42 (3.63)
95% CI of LS mean	(77.23, 93.61)
Absolute Change at Week 24 (MMRM)	
n	12
LS mean (SE)	-3.47 (3.63)
95% CI of LS mean	(-11.66, 4.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	-4.86 (3.57)
95% CI of LS mean	(-12.90, 3.17)
P-value	0.2054

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	88.38 (15.21)
Week 4 (MMRM)	
n	11
LS mean (SE)	89.39 (2.91)
95% CI of LS mean	(82.89, 95.90)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	1.01 (2.91)
95% CI of LS mean	(-5.50, 7.52)
Week 8 (MMRM)	
n	11
LS mean (SE)	90.91 (3.58)
95% CI of LS mean	(82.92, 98.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	2.53 (3.58)
95% CI of LS mean	(-5.47, 10.52)
Week 12 (MMRM)	
n	11
LS mean (SE)	91.92 (2.88)
95% CI of LS mean	(85.39, 98.45)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	3.54 (2.88)
95% CI of LS mean	(-2.99, 10.06)
Week 16 (MMRM)	
n	11
LS mean (SE)	90.40 (2.83)
95% CI of LS mean	(84.02, 96.79)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	2.02 (2.83)
95% CI of LS mean	(-4.36, 8.40)
Week 24	
n	11
Mean (SD)	93.94 (12.29)
Absolute Change at Week 24	
n	11
Mean (SD)	5.56 (10.54)
Week 24 (MMRM)	
n	11
LS mean (SE)	93.94 (2.83)
95% CI of LS mean	(87.36, 100.52)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	5.56 (2.83)
95% CI of LS mean	(-1.03, 12.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	3.79 (2.48)
95% CI of LS mean	(-1.79, 9.37)
P-value	0.1597

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	12
Mean (SD)	90.28 (11.87)
Week 4 (MMRM)	
n	12
LS mean (SE)	86.57 (2.44)
95% CI of LS mean	(81.16, 91.99)
Absolute Change at Week 4 (MMRM)	
n	12
LS mean (SE)	-3.70 (2.44)
95% CI of LS mean	(-9.12, 1.71)
Week 8 (MMRM)	
n	12
LS mean (SE)	87.96 (4.30)
95% CI of LS mean	(78.48, 97.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	12
LS mean (SE)	-2.31 (4.30)
95% CI of LS mean	(-11.80, 7.17)
Week 12 (MMRM)	
n	12
LS mean (SE)	84.26 (6.72)
95% CI of LS mean	(69.42, 99.10)
Absolute Change at Week 12 (MMRM)	
n	12
LS mean (SE)	-6.02 (6.72)
95% CI of LS mean	(-20.86, 8.82)
Week 16 (MMRM)	
n	12
LS mean (SE)	84.72 (4.47)
95% CI of LS mean	(74.87, 94.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	12
LS mean (SE)	-5.56 (4.47)
95% CI of LS mean	(-15.40, 4.29)
Week 24	
n	13
Mean (SD)	90.60 (11.65)
Absolute Change at Week 24	
n	12
Mean (SD)	-0.46 (7.66)
Week 24 (MMRM)	
n	13
LS mean (SE)	89.81 (2.17)
95% CI of LS mean	(84.98, 94.64)
Absolute Change at Week 24 (MMRM)	
n	12
LS mean (SE)	-0.46 (2.17)
95% CI of LS mean	(-5.29, 4.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	-3.01 (2.87)
95% CI of LS mean	(-9.34, 3.32)
P-value	0.3169

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	74.03 (12.84)
Week 4 (MMRM)	
n	11
LS mean (SE)	75.76 (3.40)
95% CI of LS mean	(68.15, 83.36)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	1.73 (3.40)
95% CI of LS mean	(-5.88, 9.34)
Week 8 (MMRM)	
n	11
LS mean (SE)	76.19 (4.02)
95% CI of LS mean	(67.21, 85.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	2.16 (4.02)
95% CI of LS mean	(-6.81, 11.14)
Week 12 (MMRM)	
n	11
LS mean (SE)	76.19 (3.87)
95% CI of LS mean	(67.45, 84.94)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	2.16 (3.87)
95% CI of LS mean	(-6.58, 10.91)
Week 16 (MMRM)	
n	11
LS mean (SE)	78.79 (3.34)
95% CI of LS mean	(71.26, 86.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	4.76 (3.34)
95% CI of LS mean	(-2.77, 12.29)
Week 24	
n	11
Mean (SD)	79.87 (11.54)
Absolute Change at Week 24	
n	11
Mean (SD)	5.84 (17.80)
Week 24 (MMRM)	
n	11
LS mean (SE)	79.87 (3.66)
95% CI of LS mean	(71.61, 88.13)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	5.84 (3.66)
95% CI of LS mean	(-2.41, 14.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	5.30 (3.06)
95% CI of LS mean	(-1.56, 12.16)
P-value	0.1153

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	12
Mean (SD)	68.25 (17.97)
Week 4 (MMRM)	
n	12
LS mean (SE)	66.27 (4.03)
95% CI of LS mean	(57.31, 75.23)
Absolute Change at Week 4 (MMRM)	
n	12
LS mean (SE)	-1.98 (4.03)
95% CI of LS mean	(-10.95, 6.98)
Week 8 (MMRM)	
n	12
LS mean (SE)	65.08 (5.34)
95% CI of LS mean	(53.03, 77.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	12
LS mean (SE)	-3.17 (5.34)
95% CI of LS mean	(-15.22, 8.87)
Week 12 (MMRM)	
n	12
LS mean (SE)	67.86 (4.57)
95% CI of LS mean	(57.63, 78.09)
Absolute Change at Week 12 (MMRM)	
n	12
LS mean (SE)	-0.40 (4.57)
95% CI of LS mean	(-10.62, 9.83)
Week 16 (MMRM)	
n	12
LS mean (SE)	67.86 (5.13)
95% CI of LS mean	(56.48, 79.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	12
LS mean (SE)	-0.40 (5.13)
95% CI of LS mean	(-11.77, 10.98)
Week 24	
n	13
Mean (SD)	72.53 (17.62)
Absolute Change at Week 24	
n	12
Mean (SD)	4.37 (18.44)
Week 24 (MMRM)	
n	13
LS mean (SE)	72.62 (4.86)
95% CI of LS mean	(61.81, 83.43)
Absolute Change at Week 24 (MMRM)	
n	12
LS mean (SE)	4.37 (4.86)
95% CI of LS mean	(-6.44, 15.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	1.98 (4.66)
95% CI of LS mean	(-8.39, 12.36)
P-value	0.6793

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	76.26 (18.61)
Week 4 (MMRM)	
n	11
LS mean (SE)	81.82 (6.41)
95% CI of LS mean	(67.50, 96.13)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	5.56 (6.41)
95% CI of LS mean	(-8.76, 19.87)
Week 8 (MMRM)	
n	11
LS mean (SE)	80.81 (3.73)
95% CI of LS mean	(72.34, 89.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	4.55 (3.73)
95% CI of LS mean	(-3.92, 13.02)
Week 12 (MMRM)	
n	11
LS mean (SE)	83.84 (4.43)
95% CI of LS mean	(73.84, 93.84)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	7.58 (4.43)
95% CI of LS mean	(-2.42, 17.57)
Week 16 (MMRM)	
n	11
LS mean (SE)	74.75 (5.03)
95% CI of LS mean	(63.01, 86.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	-1.52 (5.03)
95% CI of LS mean	(-13.25, 10.22)
Week 24	
n	11
Mean (SD)	82.83 (21.87)
Absolute Change at Week 24	
n	11
Mean (SD)	6.57 (10.78)
Week 24 (MMRM)	
n	11
LS mean (SE)	82.83 (3.67)
95% CI of LS mean	(74.20, 91.46)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	6.57 (3.67)
95% CI of LS mean	(-2.07, 15.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	2.53 (4.00)
95% CI of LS mean	(-7.04, 12.09)
P-value	0.5487

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	12
Mean (SD)	81.48 (20.83)
Week 4 (MMRM)	
n	12
LS mean (SE)	80.56 (4.31)
95% CI of LS mean	(71.03, 90.08)
Absolute Change at Week 4 (MMRM)	
n	12
LS mean (SE)	-0.93 (4.31)
95% CI of LS mean	(-10.46, 8.60)
Week 8 (MMRM)	
n	12
LS mean (SE)	87.04 (3.91)
95% CI of LS mean	(78.27, 95.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	12
LS mean (SE)	5.56 (3.91)
95% CI of LS mean	(-3.21, 14.32)
Week 12 (MMRM)	
n	12
LS mean (SE)	85.19 (3.09)
95% CI of LS mean	(78.30, 92.07)
Absolute Change at Week 12 (MMRM)	
n	12
LS mean (SE)	3.70 (3.09)
95% CI of LS mean	(-3.19, 10.59)
Week 16 (MMRM)	
n	12
LS mean (SE)	83.33 (7.88)
95% CI of LS mean	(65.94, 100.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	12
LS mean (SE)	1.85 (7.88)
95% CI of LS mean	(-15.54, 19.25)
Week 24	
n	13
Mean (SD)	85.47 (19.45)
Absolute Change at Week 24	
n	12
Mean (SD)	4.63 (18.63)
Week 24 (MMRM)	
n	13
LS mean (SE)	86.11 (4.93)
95% CI of LS mean	(75.17, 97.05)
Absolute Change at Week 24 (MMRM)	
n	12
LS mean (SE)	4.63 (4.93)
95% CI of LS mean	(-6.31, 15.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	3.24 (4.12)
95% CI of LS mean	(-6.08, 12.56)
P-value	0.4514

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Body (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.7487
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Body (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

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Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.5876
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Digestion (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

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Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.6182
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Eat (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-105\t-qs-mmrm-abs-cfqr-nonrd-pa-24wks-sub-test-b1-fmf.sas Creation: 06FEB2025 8:17

Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.9255
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Emotion (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.7776
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Health Perceptions (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

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Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.8032
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Physical (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

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Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: School (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.9151
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R School (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-105\t-qs-mmrm-abs-cfqr-nonrd-pa-24wks-sub-test-b1-fmf.sas Creation: 06FEB2025 8:17

Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.9211
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Treatment Burden (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-105\t-qs-mmrm-abs-cfqr-nonrd-pa-24wks-sub-test-b1-fmf.sas Creation: 06FEB2025 8:17

Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.6174
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Vitality (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-105\t-qs-mmrm-abs-cfqr-nonrd-pa-24wks-sub-test-b1-fmf.sas Creation: 06FEB2025 8:17

Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.6889
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Weight (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Program: GMA\VX121\germandossier\clinstat_prod\121-105\t-qs-mmrm-abs-cfqr-nonrd-pa-24wks-sub-test-b1-fmf.sas Creation: 06FEB2025 8:17

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	88.89 (18.59)
Week 4 (MMRM)	
n	11
LS mean (SE)	86.87 (3.58)
95% CI of LS mean	(79.28, 94.45)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	-2.02 (3.58)
95% CI of LS mean	(-9.61, 5.57)
Week 8 (MMRM)	
n	11
LS mean (SE)	93.94 (3.58)
95% CI of LS mean	(86.35, 101.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	5.05 (3.58)
95% CI of LS mean	(-2.54, 12.64)
Week 12 (MMRM)	
n	11
LS mean (SE)	90.91 (3.58)
95% CI of LS mean	(83.32, 98.49)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	2.02 (3.58)
95% CI of LS mean	(-5.57, 9.61)
Week 16 (MMRM)	
n	11
LS mean (SE)	92.93 (3.58)
95% CI of LS mean	(85.34, 100.52)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	4.04 (3.58)
95% CI of LS mean	(-3.55, 11.63)
Week 24	
n	11
Mean (SD)	91.92 (18.65)
Absolute Change at Week 24	
n	11
Mean (SD)	3.03 (7.19)
Week 24 (MMRM)	
n	11
LS mean (SE)	91.92 (3.58)
95% CI of LS mean	(84.33, 99.51)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	3.03 (3.58)
95% CI of LS mean	(-4.56, 10.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	3.54 (3.28)
95% CI of LS mean	(-3.65, 10.72)
P-value	0.3029

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	76.92 (29.90)
Week 4 (MMRM)	
n	13
LS mean (SE)	75.21 (3.86)
95% CI of LS mean	(66.78, 83.65)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	-1.71 (3.86)
95% CI of LS mean	(-10.15, 6.73)
Week 8 (MMRM)	
n	13
LS mean (SE)	77.78 (3.39)
95% CI of LS mean	(70.40, 85.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	0.85 (3.39)
95% CI of LS mean	(-6.53, 8.23)
Week 12 (MMRM)	
n	13
LS mean (SE)	78.63 (4.59)
95% CI of LS mean	(68.63, 88.64)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	1.71 (4.59)
95% CI of LS mean	(-8.29, 11.71)
Week 16 (MMRM)	
n	13
LS mean (SE)	80.34 (2.72)
95% CI of LS mean	(74.37, 86.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	3.42 (2.72)
95% CI of LS mean	(-2.55, 9.39)
Week 24	
n	13
Mean (SD)	81.20 (28.83)
Absolute Change at Week 24	
n	13
Mean (SD)	4.27 (7.23)
Week 24 (MMRM)	
n	13
LS mean (SE)	81.20 (1.99)
95% CI of LS mean	(76.83, 85.56)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	4.27 (1.99)
95% CI of LS mean	(-0.09, 8.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	3.85 (1.98)
95% CI of LS mean	(-0.50, 8.20)
P-value	0.0777

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	76.77 (19.53)
Week 4 (MMRM)	
n	11
LS mean (SE)	76.77 (3.00)
95% CI of LS mean	(70.07, 83.47)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	0.00 (3.00)
95% CI of LS mean	(-6.70, 6.70)
Week 8 (MMRM)	
n	11
LS mean (SE)	78.79 (5.81)
95% CI of LS mean	(65.76, 91.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	2.02 (5.81)
95% CI of LS mean	(-11.01, 15.05)
Week 12 (MMRM)	
n	11
LS mean (SE)	79.80 (3.54)
95% CI of LS mean	(71.74, 87.85)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	3.03 (3.54)
95% CI of LS mean	(-5.02, 11.09)
Week 16 (MMRM)	
n	11
LS mean (SE)	81.82 (4.06)
95% CI of LS mean	(72.35, 91.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	5.05 (4.06)
95% CI of LS mean	(-4.41, 14.52)
Week 24	
n	11
Mean (SD)	81.82 (15.13)
Absolute Change at Week 24	
n	11
Mean (SD)	5.05 (12.54)
Week 24 (MMRM)	
n	11
LS mean (SE)	81.82 (3.52)
95% CI of LS mean	(73.52, 90.11)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	5.05 (3.52)
95% CI of LS mean	(-3.24, 13.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	5.05 (3.57)
95% CI of LS mean	(-3.43, 13.54)
P-value	0.2010

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	85.47 (15.31)
Week 4 (MMRM)	
n	13
LS mean (SE)	87.18 (2.39)
95% CI of LS mean	(81.85, 92.51)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	1.71 (2.39)
95% CI of LS mean	(-3.62, 7.04)
Week 8 (MMRM)	
n	13
LS mean (SE)	86.32 (3.52)
95% CI of LS mean	(78.53, 94.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	0.85 (3.52)
95% CI of LS mean	(-6.94, 8.65)
Week 12 (MMRM)	
n	13
LS mean (SE)	84.62 (3.74)
95% CI of LS mean	(76.45, 92.78)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	-0.85 (3.74)
95% CI of LS mean	(-9.02, 7.31)
Week 16 (MMRM)	
n	13
LS mean (SE)	88.03 (2.96)
95% CI of LS mean	(81.44, 94.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	2.56 (2.96)
95% CI of LS mean	(-4.03, 9.16)
Week 24	
n	13
Mean (SD)	81.20 (24.17)
Absolute Change at Week 24	
n	13
Mean (SD)	-4.27 (16.06)
Week 24 (MMRM)	
n	13
LS mean (SE)	81.20 (5.84)
95% CI of LS mean	(68.33, 94.07)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	-4.27 (5.84)
95% CI of LS mean	(-17.14, 8.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	-0.85 (4.11)
95% CI of LS mean	(-10.00, 8.29)
P-value	0.8393

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	80.30 (32.33)
Week 4 (MMRM)	
n	11
LS mean (SE)	81.82 (9.10)
95% CI of LS mean	(44.14, 119.50)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	1.52 (9.10)
95% CI of LS mean	(-36.16, 39.19)
Week 8 (MMRM)	
n	11
LS mean (SE)	84.85 (8.07)
95% CI of LS mean	(44.31, 125.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	4.55 (8.07)
95% CI of LS mean	(-35.99, 45.08)
Week 12 (MMRM)	
n	11
LS mean (SE)	80.30 (8.10)
95% CI of LS mean	(50.20, 110.41)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	0.00 (8.10)
95% CI of LS mean	(-30.10, 30.10)
Week 16 (MMRM)	
n	11
LS mean (SE)	81.82 (9.97)
95% CI of LS mean	(46.06, 117.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	1.52 (9.97)
95% CI of LS mean	(-34.24, 37.27)
Week 24	
n	11
Mean (SD)	78.79 (36.58)
Absolute Change at Week 24	
n	11
Mean (SD)	-1.52 (21.67)
Week 24 (MMRM)	
n	11
LS mean (SE)	78.79 (9.63)
95% CI of LS mean	(46.17, 111.41)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	-1.52 (9.63)
95% CI of LS mean	(-34.14, 31.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	0.00 (9.75)
95% CI of LS mean	(-34.37, 34.37)
P-value	>0.9999

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	91.03 (12.94)
Week 4 (MMRM)	
n	13
LS mean (SE)	87.18 (4.29)
95% CI of LS mean	(77.79, 96.57)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	-3.85 (4.29)
95% CI of LS mean	(-13.24, 5.55)
Week 8 (MMRM)	
n	13
LS mean (SE)	91.03 (3.79)
95% CI of LS mean	(82.73, 99.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	0.00 (3.79)
95% CI of LS mean	(-8.30, 8.30)
Week 12 (MMRM)	
n	13
LS mean (SE)	87.18 (4.32)
95% CI of LS mean	(77.76, 96.60)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	-3.85 (4.32)
95% CI of LS mean	(-13.26, 5.57)
Week 16 (MMRM)	
n	13
LS mean (SE)	89.74 (3.57)
95% CI of LS mean	(81.94, 97.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	-1.28 (3.57)
95% CI of LS mean	(-9.09, 6.52)
Week 24	
n	13
Mean (SD)	91.03 (14.62)
Absolute Change at Week 24	
n	13
Mean (SD)	0.00 (9.62)
Week 24 (MMRM)	
n	13
LS mean (SE)	91.03 (2.72)
95% CI of LS mean	(85.07, 96.98)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	0.00 (2.72)
95% CI of LS mean	(-5.95, 5.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	-0.64 (2.28)
95% CI of LS mean	(-5.65, 4.37)
P-value	0.7840

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	90.91 (10.01)
Week 4 (MMRM)	
n	11
LS mean (SE)	92.12 (3.66)
95% CI of LS mean	(83.88, 100.36)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	1.21 (3.66)
95% CI of LS mean	(-7.03, 9.45)
Week 8 (MMRM)	
n	11
LS mean (SE)	92.12 (2.21)
95% CI of LS mean	(87.13, 97.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	1.21 (2.21)
95% CI of LS mean	(-3.78, 6.21)
Week 12 (MMRM)	
n	11
LS mean (SE)	92.12 (2.91)
95% CI of LS mean	(85.35, 98.89)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	1.21 (2.91)
95% CI of LS mean	(-5.56, 7.98)
Week 16 (MMRM)	
n	11
LS mean (SE)	92.73 (2.69)
95% CI of LS mean	(86.40, 99.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	1.82 (2.69)
95% CI of LS mean	(-4.51, 8.15)
Week 24	
n	11
Mean (SD)	87.88 (13.27)
Absolute Change at Week 24	
n	11
Mean (SD)	-3.03 (11.30)
Week 24 (MMRM)	
n	11
LS mean (SE)	87.88 (3.52)
95% CI of LS mean	(79.89, 95.87)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	-3.03 (3.52)
95% CI of LS mean	(-11.02, 4.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	-0.61 (2.60)
95% CI of LS mean	(-6.43, 5.22)
P-value	0.8204

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	88.72 (8.34)
Week 4 (MMRM)	
n	13
LS mean (SE)	87.69 (2.96)
95% CI of LS mean	(81.19, 94.20)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	-1.03 (2.96)
95% CI of LS mean	(-7.53, 5.48)
Week 8 (MMRM)	
n	13
LS mean (SE)	88.21 (3.09)
95% CI of LS mean	(81.41, 95.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	-0.51 (3.09)
95% CI of LS mean	(-7.30, 6.28)
Week 12 (MMRM)	
n	13
LS mean (SE)	91.28 (1.51)
95% CI of LS mean	(87.91, 94.65)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	2.56 (1.51)
95% CI of LS mean	(-0.80, 5.93)
Week 16 (MMRM)	
n	13
LS mean (SE)	90.26 (2.73)
95% CI of LS mean	(84.27, 96.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	1.54 (2.73)
95% CI of LS mean	(-4.44, 7.52)
Week 24	
n	13
Mean (SD)	87.69 (12.72)
Absolute Change at Week 24	
n	13
Mean (SD)	-1.03 (11.17)
Week 24 (MMRM)	
n	13
LS mean (SE)	87.69 (3.16)
95% CI of LS mean	(80.79, 94.60)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	-1.03 (3.16)
95% CI of LS mean	(-7.93, 5.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	0.26 (2.71)
95% CI of LS mean	(-5.69, 6.20)
P-value	0.9264

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	88.89 (14.05)
Week 4 (MMRM)	
n	11
LS mean (SE)	80.81 (2.77)
95% CI of LS mean	(74.59, 87.03)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	-8.08 (2.77)
95% CI of LS mean	(-14.30, -1.86)
Week 8 (MMRM)	
n	11
LS mean (SE)	84.85 (3.03)
95% CI of LS mean	(78.05, 91.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	-4.04 (3.03)
95% CI of LS mean	(-10.84, 2.76)
Week 12 (MMRM)	
n	11
LS mean (SE)	88.89 (3.21)
95% CI of LS mean	(81.69, 96.09)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	0.00 (3.21)
95% CI of LS mean	(-7.20, 7.20)
Week 16 (MMRM)	
n	11
LS mean (SE)	90.91 (3.05)
95% CI of LS mean	(84.02, 97.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	2.02 (3.05)
95% CI of LS mean	(-4.87, 8.91)
Week 24	
n	11
Mean (SD)	86.87 (14.76)
Absolute Change at Week 24	
n	11
Mean (SD)	-2.02 (10.91)
Week 24 (MMRM)	
n	11
LS mean (SE)	86.87 (3.14)
95% CI of LS mean	(79.87, 93.87)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	-2.02 (3.14)
95% CI of LS mean	(-9.02, 4.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	0.00 (2.22)
95% CI of LS mean	(-5.02, 5.02)
P-value	>0.9999

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	85.47 (15.31)
Week 4 (MMRM)	
n	13
LS mean (SE)	80.34 (5.55)
95% CI of LS mean	(68.21, 92.48)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	-5.13 (5.55)
95% CI of LS mean	(-17.26, 7.01)
Week 8 (MMRM)	
n	13
LS mean (SE)	80.34 (5.30)
95% CI of LS mean	(68.67, 92.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	-5.13 (5.30)
95% CI of LS mean	(-16.80, 6.55)
Week 12 (MMRM)	
n	13
LS mean (SE)	84.62 (2.68)
95% CI of LS mean	(78.52, 90.71)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	-0.85 (2.68)
95% CI of LS mean	(-6.95, 5.24)
Week 16 (MMRM)	
n	13
LS mean (SE)	82.91 (3.71)
95% CI of LS mean	(74.81, 91.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	-2.56 (3.71)
95% CI of LS mean	(-10.66, 5.53)
Week 24	
n	13
Mean (SD)	89.74 (13.95)
Absolute Change at Week 24	
n	13
Mean (SD)	4.27 (11.60)
Week 24 (MMRM)	
n	13
LS mean (SE)	89.74 (2.91)
95% CI of LS mean	(83.39, 96.10)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	4.27 (2.91)
95% CI of LS mean	(-2.08, 10.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	0.85 (2.31)
95% CI of LS mean	(-4.24, 5.95)
P-value	0.7188

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	96.59 (4.49)
Week 4 (MMRM)	
n	11
LS mean (SE)	93.18 (2.45)
95% CI of LS mean	(87.71, 98.65)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	-3.41 (2.45)
95% CI of LS mean	(-8.88, 2.06)
Week 8 (MMRM)	
n	11
LS mean (SE)	90.53 (4.15)
95% CI of LS mean	(81.28, 99.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	-6.06 (4.15)
95% CI of LS mean	(-15.31, 3.19)
Week 12 (MMRM)	
n	11
LS mean (SE)	95.83 (2.95)
95% CI of LS mean	(89.25, 102.42)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	-0.76 (2.95)
95% CI of LS mean	(-7.34, 5.83)
Week 16 (MMRM)	
n	11
LS mean (SE)	96.97 (1.88)
95% CI of LS mean	(92.76, 101.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	0.38 (1.88)
95% CI of LS mean	(-3.83, 4.58)
Week 24	
n	11
Mean (SD)	96.21 (5.73)
Absolute Change at Week 24	
n	11
Mean (SD)	-0.38 (5.42)
Week 24 (MMRM)	
n	11
LS mean (SE)	96.21 (1.65)
95% CI of LS mean	(92.51, 99.91)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	-0.38 (1.65)
95% CI of LS mean	(-4.08, 3.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	0.00 (1.68)
95% CI of LS mean	(-3.77, 3.77)
P-value	>0.9999

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	92.95 (9.97)
Week 4 (MMRM)	
n	13
LS mean (SE)	88.78 (4.40)
95% CI of LS mean	(79.20, 98.36)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	-4.17 (4.40)
95% CI of LS mean	(-13.75, 5.41)
Week 8 (MMRM)	
n	13
LS mean (SE)	87.82 (4.08)
95% CI of LS mean	(78.93, 96.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	-5.13 (4.08)
95% CI of LS mean	(-14.02, 3.76)
Week 12 (MMRM)	
n	13
LS mean (SE)	94.87 (0.87)
95% CI of LS mean	(92.76, 96.98)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	1.92 (0.87)
95% CI of LS mean	(-0.18, 4.03)
Week 16 (MMRM)	
n	13
LS mean (SE)	90.38 (3.92)
95% CI of LS mean	(81.79, 98.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	-2.56 (3.92)
95% CI of LS mean	(-11.16, 6.03)
Week 24	
n	13
Mean (SD)	91.03 (19.08)
Absolute Change at Week 24	
n	13
Mean (SD)	-1.92 (13.35)
Week 24 (MMRM)	
n	13
LS mean (SE)	91.03 (3.92)
95% CI of LS mean	(82.46, 99.59)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	-1.92 (3.92)
95% CI of LS mean	(-10.49, 6.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	-2.24 (3.02)
95% CI of LS mean	(-8.92, 4.44)
P-value	0.4739

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	85.61 (15.41)
Week 4 (MMRM)	
n	11
LS mean (SE)	80.30 (4.67)
95% CI of LS mean	(69.81, 90.79)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	-5.30 (4.67)
95% CI of LS mean	(-15.79, 5.19)
Week 8 (MMRM)	
n	11
LS mean (SE)	78.79 (4.59)
95% CI of LS mean	(68.53, 89.04)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	-6.82 (4.59)
95% CI of LS mean	(-17.07, 3.44)
Week 12 (MMRM)	
n	11
LS mean (SE)	79.04 (4.63)
95% CI of LS mean	(68.57, 89.51)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	-6.57 (4.63)
95% CI of LS mean	(-17.04, 3.90)
Week 16 (MMRM)	
n	11
LS mean (SE)	90.91 (3.83)
95% CI of LS mean	(82.15, 99.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	5.30 (3.83)
95% CI of LS mean	(-3.45, 14.06)
Week 24	
n	11
Mean (SD)	83.33 (18.63)
Absolute Change at Week 24	
n	11
Mean (SD)	-2.27 (19.75)
Week 24 (MMRM)	
n	11
LS mean (SE)	83.33 (5.43)
95% CI of LS mean	(71.20, 95.47)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	-2.27 (5.43)
95% CI of LS mean	(-14.41, 9.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	1.52 (4.44)
95% CI of LS mean	(-8.48, 11.51)
P-value	0.7407

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	85.26 (13.67)
Week 4 (MMRM)	
n	13
LS mean (SE)	82.69 (5.11)
95% CI of LS mean	(71.52, 93.87)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	-2.56 (5.11)
95% CI of LS mean	(-13.74, 8.61)
Week 8 (MMRM)	
n	13
LS mean (SE)	82.69 (4.73)
95% CI of LS mean	(72.29, 93.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	-2.56 (4.73)
95% CI of LS mean	(-12.97, 7.84)
Week 12 (MMRM)	
n	13
LS mean (SE)	85.26 (2.88)
95% CI of LS mean	(78.95, 91.56)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	0.00 (2.88)
95% CI of LS mean	(-6.30, 6.30)
Week 16 (MMRM)	
n	13
LS mean (SE)	85.26 (3.13)
95% CI of LS mean	(78.29, 92.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	0.00 (3.13)
95% CI of LS mean	(-6.96, 6.96)
Week 24	
n	13
Mean (SD)	85.90 (19.66)
Absolute Change at Week 24	
n	13
Mean (SD)	0.64 (15.39)
Week 24 (MMRM)	
n	13
LS mean (SE)	85.90 (4.30)
95% CI of LS mean	(76.52, 95.28)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	0.64 (4.30)
95% CI of LS mean	(-8.74, 10.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	0.32 (3.10)
95% CI of LS mean	(-6.49, 7.13)
P-value	0.9194

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	69.70 (21.71)
Week 4 (MMRM)	
n	11
LS mean (SE)	76.77 (5.48)
95% CI of LS mean	(64.26, 89.28)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	7.07 (5.48)
95% CI of LS mean	(-5.44, 19.58)
Week 8 (MMRM)	
n	11
LS mean (SE)	74.75 (5.40)
95% CI of LS mean	(62.48, 87.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	5.05 (5.40)
95% CI of LS mean	(-7.21, 17.31)
Week 12 (MMRM)	
n	11
LS mean (SE)	72.73 (6.83)
95% CI of LS mean	(57.39, 88.07)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	3.03 (6.83)
95% CI of LS mean	(-12.31, 18.37)
Week 16 (MMRM)	
n	11
LS mean (SE)	77.78 (5.34)
95% CI of LS mean	(65.78, 89.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	8.08 (5.34)
95% CI of LS mean	(-3.91, 20.07)
Week 24	
n	11
Mean (SD)	76.77 (20.76)
Absolute Change at Week 24	
n	11
Mean (SD)	7.07 (22.37)
Week 24 (MMRM)	
n	11
LS mean (SE)	76.77 (5.82)
95% CI of LS mean	(63.69, 89.85)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	7.07 (5.82)
95% CI of LS mean	(-6.01, 20.15)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	7.58 (5.09)
95% CI of LS mean	(-3.88, 19.04)
P-value	0.1697

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	64.96 (26.00)
Week 4 (MMRM)	
n	13
LS mean (SE)	67.52 (3.99)
95% CI of LS mean	(58.73, 76.31)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	2.56 (3.99)
95% CI of LS mean	(-6.22, 11.35)
Week 8 (MMRM)	
n	13
LS mean (SE)	75.21 (6.23)
95% CI of LS mean	(61.45, 88.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	10.26 (6.23)
95% CI of LS mean	(-3.51, 24.02)
Week 12 (MMRM)	
n	13
LS mean (SE)	70.09 (3.76)
95% CI of LS mean	(61.84, 78.33)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	5.13 (3.76)
95% CI of LS mean	(-3.12, 13.37)
Week 16 (MMRM)	
n	13
LS mean (SE)	71.79 (2.43)
95% CI of LS mean	(66.34, 77.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	6.84 (2.43)
95% CI of LS mean	(1.38, 12.30)
Week 24	
n	13
Mean (SD)	70.09 (28.10)
Absolute Change at Week 24	
n	13
Mean (SD)	5.13 (14.78)
Week 24 (MMRM)	
n	13
LS mean (SE)	70.09 (4.16)
95% CI of LS mean	(60.98, 79.19)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	5.13 (4.16)
95% CI of LS mean	(-3.97, 14.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	5.98 (2.98)
95% CI of LS mean	(-0.61, 12.58)
P-value	0.0711

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	78.79 (11.08)
Week 4 (MMRM)	
n	11
LS mean (SE)	78.79 (3.87)
95% CI of LS mean	(69.96, 87.62)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	0.00 (3.87)
95% CI of LS mean	(-8.83, 8.83)
Week 8 (MMRM)	
n	11
LS mean (SE)	78.18 (2.14)
95% CI of LS mean	(73.39, 82.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	-0.61 (2.14)
95% CI of LS mean	(-5.40, 4.19)
Week 12 (MMRM)	
n	11
LS mean (SE)	78.18 (3.05)
95% CI of LS mean	(71.36, 85.01)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	-0.61 (3.05)
95% CI of LS mean	(-7.43, 6.22)
Week 16 (MMRM)	
n	11
LS mean (SE)	83.03 (4.75)
95% CI of LS mean	(72.21, 93.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	4.24 (4.75)
95% CI of LS mean	(-6.58, 15.07)
Week 24	
n	11
Mean (SD)	77.58 (15.57)
Absolute Change at Week 24	
n	11
Mean (SD)	-1.21 (12.59)
Week 24 (MMRM)	
n	11
LS mean (SE)	77.58 (3.82)
95% CI of LS mean	(69.05, 86.10)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	-1.21 (3.82)
95% CI of LS mean	(-9.74, 7.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	1.52 (3.58)
95% CI of LS mean	(-6.64, 9.67)
P-value	0.6822

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	80.00 (14.40)
Week 4 (MMRM)	
n	13
LS mean (SE)	81.03 (4.07)
95% CI of LS mean	(72.14, 89.91)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	1.03 (4.07)
95% CI of LS mean	(-7.86, 9.91)
Week 8 (MMRM)	
n	13
LS mean (SE)	81.54 (3.09)
95% CI of LS mean	(74.77, 88.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	1.54 (3.09)
95% CI of LS mean	(-5.23, 8.31)
Week 12 (MMRM)	
n	13
LS mean (SE)	82.05 (3.02)
95% CI of LS mean	(75.42, 88.68)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	2.05 (3.02)
95% CI of LS mean	(-4.58, 8.68)
Week 16 (MMRM)	
n	13
LS mean (SE)	80.00 (4.04)
95% CI of LS mean	(71.18, 88.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	0.00 (4.04)
95% CI of LS mean	(-8.82, 8.82)
Week 24	
n	13
Mean (SD)	78.46 (15.91)
Absolute Change at Week 24	
n	13
Mean (SD)	-1.54 (12.52)
Week 24 (MMRM)	
n	13
LS mean (SE)	78.46 (3.43)
95% CI of LS mean	(70.95, 85.97)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	-1.54 (3.43)
95% CI of LS mean	(-9.05, 5.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	-0.77 (3.21)
95% CI of LS mean	(-7.81, 6.28)
P-value	0.8149

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	72.73 (29.13)
Week 4 (MMRM)	
n	11
LS mean (SE)	78.79 (6.60)
95% CI of LS mean	(63.77, 93.81)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	6.06 (6.60)
95% CI of LS mean	(-8.96, 21.08)
Week 8 (MMRM)	
n	11
LS mean (SE)	81.82 (6.81)
95% CI of LS mean	(66.39, 97.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	9.09 (6.81)
95% CI of LS mean	(-6.34, 24.52)
Week 12 (MMRM)	
n	11
LS mean (SE)	75.76 (9.70)
95% CI of LS mean	(53.97, 97.55)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	3.03 (9.70)
95% CI of LS mean	(-18.76, 24.82)
Week 16 (MMRM)	
n	11
LS mean (SE)	75.76 (8.91)
95% CI of LS mean	(55.77, 95.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	3.03 (8.91)
95% CI of LS mean	(-16.95, 23.01)
Week 24	
n	11
Mean (SD)	78.79 (34.23)
Absolute Change at Week 24	
n	11
Mean (SD)	6.06 (25.03)
Week 24 (MMRM)	
n	11
LS mean (SE)	78.79 (8.86)
95% CI of LS mean	(58.82, 98.75)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	6.06 (8.86)
95% CI of LS mean	(-13.90, 26.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	4.55 (8.46)
95% CI of LS mean	(-14.51, 23.60)
P-value	0.6038

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	56.41 (39.40)
Week 4 (MMRM)	
n	13
LS mean (SE)	64.10 (6.73)
95% CI of LS mean	(49.28, 78.93)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	7.69 (6.73)
95% CI of LS mean	(-7.14, 22.52)
Week 8 (MMRM)	
n	13
LS mean (SE)	61.54 (6.42)
95% CI of LS mean	(47.42, 75.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	5.13 (6.42)
95% CI of LS mean	(-8.99, 19.24)
Week 12 (MMRM)	
n	13
LS mean (SE)	64.10 (7.68)
95% CI of LS mean	(47.17, 81.04)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	7.69 (7.68)
95% CI of LS mean	(-9.24, 24.63)
Week 16 (MMRM)	
n	13
LS mean (SE)	58.97 (8.73)
95% CI of LS mean	(39.56, 78.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	2.56 (8.73)
95% CI of LS mean	(-16.85, 21.98)
Week 24	
n	13
Mean (SD)	61.54 (44.82)
Absolute Change at Week 24	
n	13
Mean (SD)	5.13 (18.49)
Week 24 (MMRM)	
n	13
LS mean (SE)	61.54 (5.35)
95% CI of LS mean	(49.74, 73.34)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	5.13 (5.35)
95% CI of LS mean	(-6.67, 16.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	3.85 (5.74)
95% CI of LS mean	(-8.93, 16.62)
P-value	0.5179

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period for F/MF
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Any Pulmonary Exacerbation	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 1.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period for F/MF
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Pulmonary Exacerbation Requiring Hospitalization	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 1.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period for F/MF
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Pulmonary Exacerbation Requiring IV Antibiotic Therapy	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 1.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period for F/MF
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Pulmonary Exacerbation Requiring Hospitalization or IV Antibiotic Therapy	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 1.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA
	N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

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Table 1.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

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Table 1.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA
	N = 11

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

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Table 1.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 13

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 1.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA
	N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 1.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 1.2.2.14.1
Study VX21-121-105: Subgroup Factor Test for
Time-to-First Pulmonary Exacerbation during the PEx Analysis Period for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Log-rank test.

Table 1.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 13 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.15.1
Study VX21-121-105: Subgroup Factor Test for
Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Log-rank test.

Table 1.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 1.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 13 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 1.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 1.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 1.2.2.16.1
Study VX21-121-105: Subgroup Factor Test for
Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Log-rank test.

Table 1.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 1.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 1.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 13 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 1.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.3.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 24 n (%)
Subjects with any TEAEs	22 (91.67)
Respiratory, thoracic and mediastinal disorders	17 (70.83)
Cough	11 (45.83)
Nasal congestion	4 (16.67)
Oropharyngeal pain	3 (12.50)
Infections and infestations	13 (54.17)
Upper respiratory tract infection	5 (20.83)
Gastrointestinal disorders	8 (33.33)
Abdominal pain upper	3 (12.50)
General disorders and administration site conditions	7 (29.17)
Pyrexia	4 (16.67)
Fatigue	3 (12.50)
Investigations	6 (25.00)
Nervous system disorders	4 (16.67)
Headache	3 (12.50)
Injury, poisoning and procedural complications	3 (12.50)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

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Table 1.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 24 n (%)
Subjects with any TEAEs	22 (91.67)
Grade 1/Mild	7 (29.17)
Grade 2/Moderate	15 (62.50)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Respiratory, thoracic and mediastinal disorders	17 (70.83)
Grade 1/Mild	8 (33.33)
Grade 2/Moderate	9 (37.50)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Cough	11 (45.83)
Grade 1/Mild	4 (16.67)
Grade 2/Moderate	7 (29.17)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Nasal congestion	4 (16.67)
Grade 1/Mild	4 (16.67)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 24 n (%)
Oropharyngeal pain	3 (12.50)
Grade 1/Mild	3 (12.50)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0
Infections and infestations	13 (54.17)
Grade 1/Mild	7 (29.17)
Grade 2/Moderate	6 (25.00)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Upper respiratory tract infection	5 (20.83)
Grade 1/Mild	4 (16.67)
Grade 2/Moderate	1 (4.17)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Gastrointestinal disorders	8 (33.33)
Grade 1/Mild	6 (25.00)
Grade 2/Moderate	2 (8.33)
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 24 n (%)
Abdominal pain upper	3 (12.50)
Grade 1/Mild	2 (8.33)
Grade 2/Moderate	1 (4.17)
Grade 3/Severe	0
Grade 4/Life Threatening	0
General disorders and administration site conditions	7 (29.17)
Grade 1/Mild	6 (25.00)
Grade 2/Moderate	1 (4.17)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Pyrexia	4 (16.67)
Grade 1/Mild	4 (16.67)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0
Fatigue	3 (12.50)
Grade 1/Mild	3 (12.50)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 24 n (%)
Investigations	6 (25.00)
Grade 1/Mild	5 (20.83)
Grade 2/Moderate	1 (4.17)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Nervous system disorders	4 (16.67)
Grade 1/Mild	4 (16.67)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0
Headache	3 (12.50)
Grade 1/Mild	3 (12.50)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0
Injury, poisoning and procedural complications	3 (12.50)
Grade 1/Mild	2 (8.33)
Grade 2/Moderate	1 (4.17)
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.1.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 24 n (%)

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 5% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.1.3
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 24 n (%)
Subjects with any Serious TEAEs	1 (4.17)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 5% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.1.4
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 24 n (%)

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.1.5
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events - Total and by Severity for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	0
Subjects with non-severe events (Maximum Grade 1/2)	0
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 1.3.1.6
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events - Total and by Severity for F/MF Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	1 (4.17)
Subjects with non-severe events (Maximum Grade 1/2)	1 (4.17)
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 1.3.1.7
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events - Total and by Severity for F/MF Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Subjects with any Treatment-emergent Rash Events	0
Subjects with non-severe events (Maximum Grade 1/2)	0
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 1.3.1.8
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events - Total and by Severity for F/MF Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Subjects with any Treatment-emergent Cataract Events	0
Subjects with non-severe events (Maximum Grade 1/2)	0
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 1.3.1.9
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events - Total and by Severity for F/MF Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	0
Subjects with non-severe events (Maximum Grade 1/2)	0
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 1.3.1.10
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events - Total and by Severity for F/MF Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	1 (4.17)
Subjects with non-severe events (Maximum Grade 1/2)	1 (4.17)
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 1.3.1.11
Study VX21-121-105: Summary of Death for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)

No data met the criteria for this table.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.

Table 1.3.1.12
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	3 (12.50)
Subjects with non-severe events (Maximum Grade 1/2)	3 (12.50)
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 1.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
Subjects with any TEAEs	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.1083
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-
Respiratory, thoracic and mediastinal disorders	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.4755
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 7 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 11 n (%)
Subjects with any TEAEs	9 (81.82)
Respiratory, thoracic and mediastinal disorders	7 (63.64)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 13 n (%)
Subjects with any TEAEs	13 (100.00)
Respiratory, thoracic and mediastinal disorders	10 (76.92)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 15 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 6 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.2.1
Study VX21-121-105: Subgroup Factor Test for Grade 3/4/5 TEAEs by SOC and PT for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 7 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 11 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 13 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 15 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 6 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.3.1
Study VX21-121-105: Subgroup Factor Test for Serious TEAEs by SOC and PT for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 7 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 11 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 13 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 15 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 6 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.4.1
Study VX21-121-105: Subgroup Factor Test for TEAEs Leading to Treatment Discontinuation by SOC and PT for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 7 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 11 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 13 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 15 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 6 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.5.1
Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Elevated Transaminase Events for F/MF Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.5.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.5.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.5.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 11 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.5.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 13 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.5.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.5.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 1.3.2.6.1
Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Creatine Kinase Events for F/MF Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.6.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.6.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.6.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 11 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.6.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 13 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.6.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 1.3.2.6.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.7.1
Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Rash Events for F/MF
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.7.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.7.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.7.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 11 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.7.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 13 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.7.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.7.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.8.1
Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Cataract Events for F/MF Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.8.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.8.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.8.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 11 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.8.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 13 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.8.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.8.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.9.1
Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Hypoglycemia Events for F/MF Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.9.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.9.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.9.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 11 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.9.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 13 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.9.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.9.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.10.1
Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Neuropsychiatric Events for F/MF
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 1.3.2.10.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.10.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.10.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 11 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.10.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 13 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.10.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.10.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.11.1
Study VX21-121-105: Subgroup Factor Test for Death for F/MF
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 11 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 13 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 1.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 1.3.2.12.1
Study VX21-121-105: Subgroup Factor Test for Treatment-emergent Infective Pulmonary Exacerbation Events for F/MF
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 11 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 13 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.1.1.1
Study VX21-121-105: Summary of Duration of Observation (Weeks) per Endpoint for non-(F/MF)
Full Analysis Set

Duration of observation (weeks)	VNZ/TEZ/D-IVA N = 54
Overall Study Observation Time	
n	54
Mean (SD)	24.20 (0.50)
Median	24.14
Min, Max	23.14, 25.57
$ppFEV_1$ (percentage points)	
n	54
Mean (SD)	23.51 (2.46)
Median	24.14
Min, Max	12.00, 25.57
BMI (kg/m^2)	
n	54
Mean (SD)	24.20 (0.50)
Median	24.14
Min, Max	23.14, 25.57
BMI z-score	
n	54
Mean (SD)	24.20 (0.50)
Median	24.14
Min, Max	23.14, 25.57
Sweat Chloride (mmol/L)	
n	54
Mean (SD)	23.90 (1.61)
Median	24.14
Min, Max	16.14, 25.57

- Observation duration [weeks] is defined as (date of last observation - first date of study drug in the Treatment Period +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results. For $LCI_{2.5}$, observation duration is derived from dates of accepted multiple breath washout results.

Table 2.1.1.1
Study VX21-121-105: Summary of Duration of Observation (Weeks) per Endpoint for non-(F/MF)
Full Analysis Set

Duration of observation (weeks)	VNZ/TEZ/D-IVA N = 54
Weight (kg)	
n	54
Mean (SD)	24.20 (0.50)
Median	24.14
Min, Max	23.14, 25.57
Weight z-score	
n	54
Mean (SD)	24.20 (0.50)
Median	24.14
Min, Max	23.14, 25.57
Height (cm)	
n	54
Mean (SD)	24.20 (0.50)
Median	24.14
Min, Max	23.14, 25.57
Height z-score	
n	54
Mean (SD)	24.20 (0.50)
Median	24.14
Min, Max	23.14, 25.57
CFQ-R	
n	54
Mean (SD)	24.20 (0.50)
Median	24.14
Min, Max	23.14, 25.57

- Observation duration [weeks] is defined as (date of last observation - first date of study drug in the Treatment Period +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results. For $LCI_{2.5}$, observation duration is derived from dates of accepted multiple breath washout results.

Table 2.1.1.1
Study VX21-121-105: Summary of Duration of Observation (Weeks) per Endpoint for non-(F/MF)
Full Analysis Set

Duration of observation (weeks)	VNZ/TEZ/D-IVA N = 54
Pulmonary Exacerbation	
n	54
Mean (SD)	24.20 (0.50)
Median	24.14
Min, Max	23.14, 25.57
$LCI_{2.5}$	
n	53
Mean (SD)	22.65 (4.60)
Median	24.14
Min, Max	3.86, 25.57
Safety	
n	54
Mean (SD)	23.95 (1.96)
Median	24.14
Min, Max	10.29, 25.57

- Observation duration [weeks] is defined as (date of last observation - first date of study drug in the Treatment Period +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results. For $LCI_{2.5}$, observation duration is derived from dates of accepted multiple breath washout results.

Table 2.1.2.1
Study VX21-121-105: Summary of Patients with Ongoing Antibiotic Medications at Baseline or at Week 24 non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline, N1	54
Subjects with 0 ongoing AB	46 (85.19)
Subjects with 1 ongoing AB	8 (14.81)
Subjects with ≥ 2 ongoing AB	0
Subjects with ≥ 1 ongoing IV AB	0
Week 24, N1	54
Subjects with 0 ongoing AB	49 (90.74)
Subjects with 1 ongoing AB	5 (9.26)
Subjects with ≥ 2 ongoing AB	0
Subjects with ≥ 1 ongoing IV AB	0

- AB: Antibiotic medications are defined as those medications with the ATC level 2 names of "ANTIBACTERIALS FOR SYSTEMIC USE" and "ANTIMYCOBACTERIALS".
- Antibiotic medications included in this summary refer to those with route being "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- IV antibiotic medications refer to those with route being "INTRAVENOUS" or "INTRAVENOUS BOLUS".
- The ongoing antibiotic medications at baseline refer to those with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing antibiotic medications at Week 24 refer to those with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 2.1.2.2
Study VX21-121-105: Summary of Patients with Antibiotic Medications during the Study Treatment Period non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
All subjects	54
Subjects with 0 AB	24 (44.44)
Subjects with 1-3 AB	28 (51.85)
Subjects with ≥ 4 AB	2 (3.70)
Subjects with 0 IV AB	51 (94.44)
Subjects with 1 IV AB	3 (5.56)
Subjects with ≥ 2 IV AB	0
Subjects with 0 ongoing antibiotic medication at baseline	46
Subjects with 0 AB	24 (52.17)
Subjects with 1-3 AB	21 (45.65)
Subjects with ≥ 4 AB	1 (2.17)
Subjects with 0 IV AB	43 (93.48)
Subjects with 1 IV AB	3 (6.52)
Subjects with ≥ 2 IV AB	0

- AB: Antibiotic medications are defined as those medications with the ATC level 2 names of "ANTIBACTERIALS FOR SYSTEMIC USE" and "ANTIMYCOBACTERIALS".
- Antibiotic medications included in this summary refer to those with route being "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- IV antibiotic medications refer to those with route being "INTRAVENOUS" or "INTRAVENOUS BOLUS".
- Antibiotic medications during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period, and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 2.1.3.1
Study VX21-121-105: Summary of Patients with Ongoing Physiotherapies at Baseline or at Week 24 non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline, N1	54
Subjects with 0 ongoing PT	12 (22.22)
Subjects with 1 ongoing PT	37 (68.52)
Subjects with ≥ 2 ongoing PT	5 (9.26)
Week 24, N1	54
Subjects with 0 ongoing PT	12 (22.22)
Subjects with 1 ongoing PT	37 (68.52)
Subjects with ≥ 2 ongoing PT	5 (9.26)

- PT: Physiotherapies refer to the non-pharmacological treatments with preferred names of "Positive expiratory pressure therapy", "Airway secretion clearance therapy", "Positive end-expiratory pressure", or "Physiotherapy chest".
- The ongoing physiotherapy at baseline is defined as a physiotherapy whose start date is prior to first dose date of study drug in the Treatment Period and the end date is ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing physiotherapy at Week 24 is defined as a physiotherapy whose start date is prior to Week 24 visit date and the end date is ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 2.1.3.2
Study VX21-121-105: Summary of Patients with Physiotherapies during the Study Treatment Period non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
All subjects	54
Subjects with 0 PT	12 (22.22)
Subjects with 1 PT	37 (68.52)
Subjects with ≥ 2 PT	5 (9.26)
Subjects with 0 ongoing physiotherapies at baseline	12
Subjects with 0 PT	12 (100.00)
Subjects with 1 PT	0
Subjects with ≥ 2 PT	0

- PT: Physiotherapies refer to the non-pharmacological treatments with preferred names of "Positive expiratory pressure therapy", "Airway secretion clearance therapy", "Positive end-expiratory pressure", or "Physiotherapy chest".
- Physiotherapies during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period, and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 2.1.4.1
Study VX21-121-105: Summary of Patients with Ongoing Inhaled Medications at Baseline or at Week 24 non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline, N1	54
Subjects with 0 ongoing IM	4 (7.41)
Subjects with 1 ongoing IM	6 (11.11)
Subjects with ≥ 2 ongoing IM	44 (81.48)
Week 24, N1	54
Subjects with 0 ongoing IM	4 (7.41)
Subjects with 1 ongoing IM	6 (11.11)
Subjects with ≥ 2 ongoing IM	44 (81.48)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB) and for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 24 refer to those IMs with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 2.1.4.2
Study VX21-121-105: Summary of Patients with Inhaled Medications during the Study Treatment Period non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
All subjects	54
Subjects with 0 IM	4 (7.41)
Subjects with 1 IM	6 (11.11)
Subjects with ≥ 2 IM	44 (81.48)
Subjects with 0 ongoing inhaled medication at baseline	4
Subjects with 0 IM	4 (100.00)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	0

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB) and for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 2.1.4.3
Study VX21-121-105: Summary of Patients with Ongoing Inhaled Medications for Mucolytics at Baseline or at Week 24 non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline, N1	54
Subjects with 0 ongoing IM	9 (16.67)
Subjects with 1 ongoing IM	19 (35.19)
Subjects with ≥ 2 ongoing IM	26 (48.15)
Week 24, N1	54
Subjects with 0 ongoing IM	9 (16.67)
Subjects with 1 ongoing IM	19 (35.19)
Subjects with ≥ 2 ongoing IM	26 (48.15)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 24 refer to those IMs with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 2.1.4.4
Study VX21-121-105: Summary of Patients with Inhaled Medications for Mucolytics during the Study Treatment Period non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
All subjects	54
Subjects with 0 IM	9 (16.67)
Subjects with 1 IM	19 (35.19)
Subjects with ≥ 2 IM	26 (48.15)
Subjects with 0 ongoing inhaled medication at baseline	9
Subjects with 0 IM	9 (100.00)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	0

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 2.1.4.5
Study VX21-121-105: Summary of Patients with Ongoing Inhaled Medications for Obstructive Airway Disease at Baseline or at Week 24 non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline, N1	54
Subjects with 0 ongoing IM	13 (24.07)
Subjects with 1 ongoing IM	24 (44.44)
Subjects with ≥ 2 ongoing IM	17 (31.48)
Week 24, N1	54
Subjects with 0 ongoing IM	13 (24.07)
Subjects with 1 ongoing IM	23 (42.59)
Subjects with ≥ 2 ongoing IM	18 (33.33)

- IM: Inhaled medications refer to those medications for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 24 refer to those IMs with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 2.1.4.6

Study VX21-121-105: Summary of Patients with Inhaled Medications for Obstructive Airway Disease during the Study Treatment Period non-(F/MF)

Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
All subjects	54
Subjects with 0 IM	13 (24.07)
Subjects with 1 IM	23 (42.59)
Subjects with ≥ 2 IM	18 (33.33)
Subjects with 0 ongoing inhaled medication at baseline	13
Subjects with 0 IM	13 (100.00)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	0

- IM: Inhaled medications refer to those medications for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing..
- The percentages in this table are calculated based on the number of subjects under each category.

Table 2.1.5.1
Study VX21-121-105: Summary of Patients with Ongoing CF-related Medications at Baseline or at Week 24 non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline, N1	54
Subjects with 0 ongoing CF-related medications	1 (1.85)
Subjects with 1 ongoing CF-related medications	3 (5.56)
Subjects with 2 ongoing CF-related medications	2 (3.70)
Subjects with 3 ongoing CF-related medications	10 (18.52)
Subjects with 4 ongoing CF-related medications	12 (22.22)
Subjects with ≥5 ongoing CF-related medications	26 (48.15)
Week 24, N1	54
Subjects with 0 ongoing CF-related medications	1 (1.85)
Subjects with 1 ongoing CF-related medications	3 (5.56)
Subjects with 2 ongoing CF-related medications	4 (7.41)
Subjects with 3 ongoing CF-related medications	11 (20.37)
Subjects with 4 ongoing CF-related medications	12 (22.22)
Subjects with ≥5 ongoing CF-related medications	23 (42.59)

- CF-related medications: CF co-medications are defined as those medications with
o ATC level 2 names of "DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES", "DIGESTIVES, INCL. ENZYMES", "ANTIBACTERIALS FOR SYSTEMIC USE", "DRUGS USED IN DIABETES", "BILE AND LIVER THERAPY", "GENERAL NUTRIENTS";
o or ATC level 3 names of "DRUGS FOR CONSTIPATION", "PROPULSIVES";
o or ATC level 4 names of "MUCOLYTICS".
In addition, the route of administration for "DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES" and "MUCOLYTICS" requires to be "RESPIRATORY (INHALATION)" and the route for "ANTIBACTERIALS FOR SYSTEMIC USE" requires to be "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- The ongoing CF-related medications at baseline refer to those CF-related medications with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing CF-related medications at Week 24 refer to those CF-related medications with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.
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Table 2.2.1.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	53
Mean (SD)	102.11 (10.58)
Week 24	
n	50
Mean (SD)	101.07 (11.55)
Absolute Change at Week 24	
n	49
Mean (SD)	-1.83 (8.92)
Absolute Change through Week 24 (MMRM)	
n	52
LS mean (SE)	-0.91 (1.14)
95% CI of LS mean	(-3.20, 1.38)
P-value	0.4292

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline ppFEV$_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	16.77 (2.14)
Week 24	
n	54
Mean (SD)	17.02 (2.45)
Absolute Change at Week 24	
n	54
Mean (SD)	0.24 (0.77)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	0.24 (0.10)
95% CI of LS mean	(0.04, 0.45)
P-value	0.0226

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.1.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	0.07 (0.86)
Week 24	
n	54
Mean (SD)	0.04 (0.93)
Absolute Change at Week 24	
n	54
Mean (SD)	-0.03 (0.31)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	-0.03 (0.04)
95% CI of LS mean	(-0.12, 0.05)
P-value	0.4250

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.1.4.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	35.22 (19.72)
Week 24	
n	52
Mean (SD)	27.88 (13.38)
Absolute Change at Week 24	
n	52
Mean (SD)	-7.53 (15.15)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	-7.87 (1.41)
95% CI of LS mean	(-10.70, -5.03)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.4.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Non-missing value at Week 24, N1	52
Number of subjects with missing value at Week 24	2
SwCl <60 mmol/L at Week 24, n (%)	51 (94.44)
95% CI for the proportion	(84.61, 98.84)

- N1: number of subjects with non-missing SwCl at Week 24
- n: number of subjects with SwCl <60 mmol/L
- 95% CI is based on the Clopper-Pearson method

Table 2.2.1.4.3
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Non-missing value at Week 24, N1	52
Number of subjects with missing value at Week 24	2
SwCl <30 mmol/L at Week 24, n (%)	33 (61.11)
95% CI for the proportion	(46.88, 74.08)

- N1: number of subjects with non-missing SwCl at Week 24
- n: number of subjects with SwCl <30 mmol/L
- 95% CI is based on the Clopper-Pearson method

Table 2.2.1.5
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	29.98 (8.23)
Week 24	
n	54
Mean (SD)	31.68 (9.01)
Absolute Change at Week 24	
n	54
Mean (SD)	1.70 (1.61)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	1.70 (0.21)
95% CI of LS mean	(1.28, 2.12)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.1.6
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	0.01 (0.91)
Week 24	
n	54
Mean (SD)	0.00 (0.96)
Absolute Change at Week 24	
n	54
Mean (SD)	-0.01 (0.23)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	-0.01 (0.03)
95% CI of LS mean	(-0.07, 0.05)
P-value	0.7305

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.1.7
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	132.36 (11.03)
Week 24	
n	54
Mean (SD)	135.05 (11.24)
Absolute Change at Week 24	
n	54
Mean (SD)	2.69 (1.08)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	2.69 (0.15)
95% CI of LS mean	(2.40, 2.98)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.1.8
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	-0.01 (0.96)
Week 24	
n	54
Mean (SD)	-0.01 (0.98)
Absolute Change at Week 24	
n	54
Mean (SD)	0.00 (0.18)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	0.00 (0.02)
95% CI of LS mean	(-0.05, 0.05)
P-value	0.9226

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.1.9
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	51
Mean (SD)	6.51 (0.53)
Week 24	
n	44
Mean (SD)	6.46 (0.52)
Absolute Change at Week 24	
n	42
Mean (SD)	-0.14 (0.52)
Absolute Change through Week 24 (MMRM)	
n	42
LS mean (SE)	-0.08 (0.06)
95% CI of LS mean	(-0.19, 0.04)
P-value	0.1827

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

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Table 2.2.1.10.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	52
Mean (SD)	82.53 (18.25)
Week 4 (MMRM)	
n	52
LS mean (SE)	83.33 (2.30)
95% CI of LS mean	(78.72, 87.95)
Absolute Change at Week 4 (MMRM)	
n	52
LS mean (SE)	0.80 (2.30)
95% CI of LS mean	(-3.82, 5.42)
Week 8 (MMRM)	
n	52
LS mean (SE)	85.10 (2.29)
95% CI of LS mean	(80.51, 89.69)
Absolute Change at Week 8 (MMRM)	
n	52
LS mean (SE)	2.56 (2.29)
95% CI of LS mean	(-2.03, 7.15)
Week 12 (MMRM)	
n	51
LS mean (SE)	89.85 (1.72)
95% CI of LS mean	(86.40, 93.30)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Absolute Change at Week 12 (MMRM)	
n	51
LS mean (SE)	7.32 (1.72)
95% CI of LS mean	(3.87, 10.77)
Week 16 (MMRM)	
n	52
LS mean (SE)	90.54 (1.76)
95% CI of LS mean	(87.01, 94.08)
Absolute Change at Week 16 (MMRM)	
n	52
LS mean (SE)	8.01 (1.76)
95% CI of LS mean	(4.48, 11.55)
Week 24	
n	54
Mean (SD)	84.26 (17.26)
Absolute Change at Week 24	
n	52
Mean (SD)	2.88 (21.32)
Week 24 (MMRM)	
n	54
LS mean (SE)	85.42 (2.21)
95% CI of LS mean	(80.99, 89.84)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Absolute Change at Week 24 (MMRM)	
n	52
LS mean (SE)	2.88 (2.21)
95% CI of LS mean	(-1.54, 7.31)
Absolute Change through Week 24 (MMRM)	
n	52
LS mean (SE)	5.45 (1.63)
95% CI of LS mean	(2.18, 8.71)
P-value	0.0015

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Respiration

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	52 (96.30)
Week 4	52 (96.30)
Absolute Change at Week 4	52 (96.30)
Week 8	52 (96.30)
Absolute Change at Week 8	52 (96.30)
Week 12	51 (94.44)
Absolute Change at Week 12	51 (94.44)
Week 16	52 (96.30)
Absolute Change at Week 16	52 (96.30)
Week 24	54 (100.00)
Absolute Change at Week 24	52 (96.30)
Through Week 24	54 (100.00)
Absolute Change through Week 24	52 (96.30)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	52 (96.30)
Week 4	52 (96.30)
Absolute Change at Week 4	52 (96.30)
Week 8	52 (96.30)
Absolute Change at Week 8	52 (96.30)
Week 12	51 (94.44)
Absolute Change at Week 12	51 (94.44)
Week 16	52 (96.30)
Absolute Change at Week 16	52 (96.30)
Week 24	54 (100.00)
Absolute Change at Week 24	52 (96.30)
Through Week 24	54 (100.00)
Absolute Change through Week 24	52 (96.30)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	51 (94.44)
Week 4	52 (96.30)
Absolute Change at Week 4	51 (94.44)
Week 8	52 (96.30)
Absolute Change at Week 8	51 (94.44)
Week 12	51 (94.44)
Absolute Change at Week 12	50 (92.59)
Week 16	52 (96.30)
Absolute Change at Week 16	51 (94.44)
Week 24	54 (100.00)
Absolute Change at Week 24	51 (94.44)
Through Week 24	54 (100.00)
Absolute Change through Week 24	51 (94.44)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	52 (96.30)
Week 4	52 (96.30)
Absolute Change at Week 4	52 (96.30)
Week 8	52 (96.30)
Absolute Change at Week 8	52 (96.30)
Week 12	51 (94.44)
Absolute Change at Week 12	51 (94.44)
Week 16	52 (96.30)
Absolute Change at Week 16	52 (96.30)
Week 24	54 (100.00)
Absolute Change at Week 24	52 (96.30)
Through Week 24	54 (100.00)
Absolute Change through Week 24	52 (96.30)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	52 (96.30)
Week 4	52 (96.30)
Absolute Change at Week 4	52 (96.30)
Week 8	52 (96.30)
Absolute Change at Week 8	52 (96.30)
Week 12	51 (94.44)
Absolute Change at Week 12	51 (94.44)
Week 16	52 (96.30)
Absolute Change at Week 16	52 (96.30)
Week 24	54 (100.00)
Absolute Change at Week 24	52 (96.30)
Through Week 24	54 (100.00)
Absolute Change through Week 24	52 (96.30)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	52 (96.30)
Week 4	52 (96.30)
Absolute Change at Week 4	52 (96.30)
Week 8	52 (96.30)
Absolute Change at Week 8	52 (96.30)
Week 12	51 (94.44)
Absolute Change at Week 12	51 (94.44)
Week 16	52 (96.30)
Absolute Change at Week 16	52 (96.30)
Week 24	54 (100.00)
Absolute Change at Week 24	52 (96.30)
Through Week 24	54 (100.00)
Absolute Change through Week 24	52 (96.30)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Social

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	52 (96.30)
Week 4	52 (96.30)
Absolute Change at Week 4	52 (96.30)
Week 8	52 (96.30)
Absolute Change at Week 8	52 (96.30)
Week 12	51 (94.44)
Absolute Change at Week 12	51 (94.44)
Week 16	52 (96.30)
Absolute Change at Week 16	52 (96.30)
Week 24	54 (100.00)
Absolute Change at Week 24	52 (96.30)
Through Week 24	54 (100.00)
Absolute Change through Week 24	52 (96.30)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	52 (96.30)
Week 4	52 (96.30)
Absolute Change at Week 4	52 (96.30)
Week 8	52 (96.30)
Absolute Change at Week 8	52 (96.30)
Week 12	51 (94.44)
Absolute Change at Week 12	51 (94.44)
Week 16	52 (96.30)
Absolute Change at Week 16	52 (96.30)
Week 24	54 (100.00)
Absolute Change at Week 24	52 (96.30)
Through Week 24	54 (100.00)
Absolute Change through Week 24	52 (96.30)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	85.51 (17.70)
Week 4 (MMRM)	
n	54
LS mean (SE)	85.08 (2.49)
95% CI of LS mean	(80.09, 90.07)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	-0.43 (2.49)
95% CI of LS mean	(-5.42, 4.56)
Week 8 (MMRM)	
n	54
LS mean (SE)	86.73 (2.09)
95% CI of LS mean	(82.54, 90.92)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	1.21 (2.09)
95% CI of LS mean	(-2.97, 5.40)
Week 12 (MMRM)	
n	53
LS mean (SE)	91.80 (1.72)
95% CI of LS mean	(88.36, 95.24)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.1.10.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	6.29 (1.72)
95% CI of LS mean	(2.84, 9.73)
Week 16 (MMRM)	
n	54
LS mean (SE)	91.11 (1.95)
95% CI of LS mean	(87.20, 95.02)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	5.60 (1.95)
95% CI of LS mean	(1.68, 9.51)
Week 24	
n	54
Mean (SD)	86.42 (17.19)
Absolute Change at Week 24	
n	54
Mean (SD)	0.91 (22.98)
Week 24 (MMRM)	
n	54
LS mean (SE)	86.42 (2.33)
95% CI of LS mean	(81.75, 91.09)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	0.91 (2.33)
95% CI of LS mean	(-3.76, 5.57)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	3.25 (1.75)
95% CI of LS mean	(-0.25, 6.75)
P-value	0.0682

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Respiration

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Health Perception

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: School

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Vitality

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Weight

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	52
Mean (SD)	79.06 (25.34)
Week 4 (MMRM)	
n	52
LS mean (SE)	82.05 (2.78)
95% CI of LS mean	(76.47, 87.63)
Absolute Change at Week 4 (MMRM)	
n	52
LS mean (SE)	2.99 (2.78)
95% CI of LS mean	(-2.59, 8.57)
Week 8 (MMRM)	
n	52
LS mean (SE)	86.32 (2.50)
95% CI of LS mean	(81.30, 91.35)
Absolute Change at Week 8 (MMRM)	
n	52
LS mean (SE)	7.26 (2.50)
95% CI of LS mean	(2.24, 12.29)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	51
LS mean (SE)	87.79 (2.23)
95% CI of LS mean	(83.31, 92.27)
Absolute Change at Week 12 (MMRM)	
n	51
LS mean (SE)	8.73 (2.23)
95% CI of LS mean	(4.25, 13.21)
Week 16 (MMRM)	
n	52
LS mean (SE)	89.74 (2.02)
95% CI of LS mean	(85.68, 93.80)
Absolute Change at Week 16 (MMRM)	
n	52
LS mean (SE)	10.68 (2.02)
95% CI of LS mean	(6.62, 14.74)
Week 24	
n	54
Mean (SD)	85.19 (23.25)
Absolute Change at Week 24	
n	52
Mean (SD)	5.77 (27.35)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	84.83 (3.04)
95% CI of LS mean	(78.72, 90.93)
Absolute Change at Week 24 (MMRM)	
n	52
LS mean (SE)	5.77 (3.04)
95% CI of LS mean	(-0.34, 11.87)
Absolute Change through Week 24 (MMRM)	
n	52
LS mean (SE)	8.23 (2.24)
95% CI of LS mean	(3.72, 12.73)
P-value	0.0006

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	51
Mean (SD)	79.08 (22.07)
Week 4 (MMRM)	
n	52
LS mean (SE)	71.90 (4.14)
95% CI of LS mean	(63.59, 80.20)
Absolute Change at Week 4 (MMRM)	
n	51
LS mean (SE)	-7.19 (4.14)
95% CI of LS mean	(-15.50, 1.12)
Week 8 (MMRM)	
n	52
LS mean (SE)	76.47 (3.38)
95% CI of LS mean	(69.67, 83.27)
Absolute Change at Week 8 (MMRM)	
n	51
LS mean (SE)	-2.61 (3.38)
95% CI of LS mean	(-9.41, 4.18)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	51
LS mean (SE)	78.98 (2.87)
95% CI of LS mean	(73.22, 84.74)
Absolute Change at Week 12 (MMRM)	
n	50
LS mean (SE)	-0.10 (2.87)
95% CI of LS mean	(-5.87, 5.66)
Week 16 (MMRM)	
n	52
LS mean (SE)	82.35 (3.10)
95% CI of LS mean	(76.13, 88.58)
Absolute Change at Week 16 (MMRM)	
n	51
LS mean (SE)	3.27 (3.10)
95% CI of LS mean	(-2.96, 9.49)
Week 24	
n	54
Mean (SD)	83.33 (23.12)
Absolute Change at Week 24	
n	51
Mean (SD)	3.92 (25.51)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	83.01 (3.06)
95% CI of LS mean	(76.85, 89.16)
Absolute Change at Week 24 (MMRM)	
n	51
LS mean (SE)	3.92 (3.06)
95% CI of LS mean	(-2.23, 10.08)
Absolute Change through Week 24 (MMRM)	
n	51
LS mean (SE)	3.59 (2.64)
95% CI of LS mean	(-1.72, 8.91)
P-value	0.1800

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	52
Mean (SD)	78.21 (22.33)
Week 4 (MMRM)	
n	52
LS mean (SE)	79.27 (2.55)
95% CI of LS mean	(74.15, 84.40)
Absolute Change at Week 4 (MMRM)	
n	52
LS mean (SE)	1.07 (2.55)
95% CI of LS mean	(-4.05, 6.19)
Week 8 (MMRM)	
n	52
LS mean (SE)	76.92 (2.58)
95% CI of LS mean	(71.74, 82.11)
Absolute Change at Week 8 (MMRM)	
n	52
LS mean (SE)	-1.28 (2.58)
95% CI of LS mean	(-6.47, 3.90)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	51
LS mean (SE)	82.90 (2.68)
95% CI of LS mean	(77.52, 88.29)
Absolute Change at Week 12 (MMRM)	
n	51
LS mean (SE)	4.70 (2.68)
95% CI of LS mean	(-0.69, 10.09)
Week 16 (MMRM)	
n	52
LS mean (SE)	84.19 (2.37)
95% CI of LS mean	(79.43, 88.94)
Absolute Change at Week 16 (MMRM)	
n	52
LS mean (SE)	5.98 (2.37)
95% CI of LS mean	(1.23, 10.74)
Week 24	
n	54
Mean (SD)	87.65 (18.65)
Absolute Change at Week 24	
n	52
Mean (SD)	9.40 (18.33)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	87.61 (2.09)
95% CI of LS mean	(83.41, 91.80)
Absolute Change at Week 24 (MMRM)	
n	52
LS mean (SE)	9.40 (2.09)
95% CI of LS mean	(5.21, 13.60)
Absolute Change through Week 24 (MMRM)	
n	52
LS mean (SE)	7.69 (1.85)
95% CI of LS mean	(3.99, 11.40)
P-value	0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	52
Mean (SD)	73.00 (15.09)
Week 4 (MMRM)	
n	52
LS mean (SE)	73.34 (1.85)
95% CI of LS mean	(69.63, 77.05)
Absolute Change at Week 4 (MMRM)	
n	52
LS mean (SE)	0.34 (1.85)
95% CI of LS mean	(-3.36, 4.05)
Week 8 (MMRM)	
n	52
LS mean (SE)	75.64 (1.88)
95% CI of LS mean	(71.86, 79.43)
Absolute Change at Week 8 (MMRM)	
n	52
LS mean (SE)	2.64 (1.88)
95% CI of LS mean	(-1.14, 6.43)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	51
LS mean (SE)	77.57 (1.91)
95% CI of LS mean	(73.73, 81.41)
Absolute Change at Week 12 (MMRM)	
n	51
LS mean (SE)	4.57 (1.91)
95% CI of LS mean	(0.73, 8.41)
Week 16 (MMRM)	
n	52
LS mean (SE)	79.81 (1.94)
95% CI of LS mean	(75.91, 83.70)
Absolute Change at Week 16 (MMRM)	
n	52
LS mean (SE)	6.81 (1.94)
95% CI of LS mean	(2.92, 10.70)
Week 24	
n	54
Mean (SD)	78.47 (15.07)
Absolute Change at Week 24	
n	52
Mean (SD)	6.01 (12.77)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	79.01 (1.61)
95% CI of LS mean	(75.77, 82.24)
Absolute Change at Week 24 (MMRM)	
n	52
LS mean (SE)	6.01 (1.61)
95% CI of LS mean	(2.77, 9.25)
Absolute Change through Week 24 (MMRM)	
n	52
LS mean (SE)	6.41 (1.58)
95% CI of LS mean	(3.24, 9.58)
P-value	0.0002

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	52
Mean (SD)	86.32 (12.90)
Week 4 (MMRM)	
n	52
LS mean (SE)	86.54 (1.84)
95% CI of LS mean	(82.84, 90.24)
Absolute Change at Week 4 (MMRM)	
n	52
LS mean (SE)	0.21 (1.84)
95% CI of LS mean	(-3.49, 3.92)
Week 8 (MMRM)	
n	52
LS mean (SE)	83.80 (2.30)
95% CI of LS mean	(79.19, 88.42)
Absolute Change at Week 8 (MMRM)	
n	52
LS mean (SE)	-2.52 (2.30)
95% CI of LS mean	(-7.13, 2.09)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	51
LS mean (SE)	85.53 (2.11)
95% CI of LS mean	(81.31, 89.76)
Absolute Change at Week 12 (MMRM)	
n	51
LS mean (SE)	-0.79 (2.11)
95% CI of LS mean	(-5.02, 3.44)
Week 16 (MMRM)	
n	52
LS mean (SE)	89.00 (2.05)
95% CI of LS mean	(84.88, 93.11)
Absolute Change at Week 16 (MMRM)	
n	52
LS mean (SE)	2.67 (2.05)
95% CI of LS mean	(-1.45, 6.79)
Week 24	
n	54
Mean (SD)	89.61 (15.49)
Absolute Change at Week 24	
n	52
Mean (SD)	3.74 (16.01)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	90.06 (1.99)
95% CI of LS mean	(86.08, 94.05)
Absolute Change at Week 24 (MMRM)	
n	52
LS mean (SE)	3.74 (1.99)
95% CI of LS mean	(-0.25, 7.73)
Absolute Change through Week 24 (MMRM)	
n	52
LS mean (SE)	3.21 (1.68)
95% CI of LS mean	(-0.16, 6.57)
P-value	0.0617

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Social

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	52
Mean (SD)	65.20 (20.52)
Week 4 (MMRM)	
n	52
LS mean (SE)	66.94 (1.99)
95% CI of LS mean	(62.93, 70.95)
Absolute Change at Week 4 (MMRM)	
n	52
LS mean (SE)	1.74 (1.99)
95% CI of LS mean	(-2.27, 5.75)
Week 8 (MMRM)	
n	52
LS mean (SE)	68.41 (2.23)
95% CI of LS mean	(63.93, 72.88)
Absolute Change at Week 8 (MMRM)	
n	52
LS mean (SE)	3.21 (2.23)
95% CI of LS mean	(-1.27, 7.68)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Social

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	51
LS mean (SE)	72.64 (2.11)
95% CI of LS mean	(68.40, 76.87)
Absolute Change at Week 12 (MMRM)	
n	51
LS mean (SE)	7.43 (2.11)
95% CI of LS mean	(3.20, 11.67)
Week 16 (MMRM)	
n	52
LS mean (SE)	72.53 (2.54)
95% CI of LS mean	(67.42, 77.63)
Absolute Change at Week 16 (MMRM)	
n	52
LS mean (SE)	7.33 (2.54)
95% CI of LS mean	(2.22, 12.43)
Week 24	
n	54
Mean (SD)	74.43 (15.49)
Absolute Change at Week 24	
n	52
Mean (SD)	10.26 (20.60)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Social

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	75.46 (1.97)
95% CI of LS mean	(71.49, 79.43)
Absolute Change at Week 24 (MMRM)	
n	52
LS mean (SE)	10.26 (1.97)
95% CI of LS mean	(6.29, 14.23)
Absolute Change through Week 24 (MMRM)	
n	52
LS mean (SE)	8.79 (2.06)
95% CI of LS mean	(4.65, 12.94)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	52
Mean (SD)	75.21 (21.96)
Week 4 (MMRM)	
n	52
LS mean (SE)	78.21 (2.29)
95% CI of LS mean	(73.61, 82.80)
Absolute Change at Week 4 (MMRM)	
n	52
LS mean (SE)	2.99 (2.29)
95% CI of LS mean	(-1.60, 7.58)
Week 8 (MMRM)	
n	52
LS mean (SE)	77.67 (2.41)
95% CI of LS mean	(72.83, 82.52)
Absolute Change at Week 8 (MMRM)	
n	52
LS mean (SE)	2.46 (2.41)
95% CI of LS mean	(-2.39, 7.30)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	51
LS mean (SE)	79.26 (2.55)
95% CI of LS mean	(74.14, 84.37)
Absolute Change at Week 12 (MMRM)	
n	51
LS mean (SE)	4.04 (2.55)
95% CI of LS mean	(-1.07, 9.16)
Week 16 (MMRM)	
n	52
LS mean (SE)	79.70 (2.83)
95% CI of LS mean	(74.01, 85.39)
Absolute Change at Week 16 (MMRM)	
n	52
LS mean (SE)	4.49 (2.83)
95% CI of LS mean	(-1.20, 10.18)
Week 24	
n	54
Mean (SD)	80.66 (21.93)
Absolute Change at Week 24	
n	52
Mean (SD)	5.34 (21.73)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	80.56 (2.67)
95% CI of LS mean	(75.20, 85.91)
Absolute Change at Week 24 (MMRM)	
n	52
LS mean (SE)	5.34 (2.67)
95% CI of LS mean	(-0.02, 10.70)
Absolute Change through Week 24 (MMRM)	
n	52
LS mean (SE)	4.91 (2.43)
95% CI of LS mean	(0.03, 9.79)
P-value	0.0484

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	79.12 (26.50)
Week 4 (MMRM)	
n	54
LS mean (SE)	81.69 (1.92)
95% CI of LS mean	(77.84, 85.54)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	2.57 (1.92)
95% CI of LS mean	(-1.28, 6.42)
Week 8 (MMRM)	
n	54
LS mean (SE)	81.28 (2.28)
95% CI of LS mean	(76.71, 85.84)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	2.16 (2.28)
95% CI of LS mean	(-2.41, 6.73)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	84.11 (2.01)
95% CI of LS mean	(80.07, 88.15)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	5.00 (2.01)
95% CI of LS mean	(0.96, 9.04)
Week 16 (MMRM)	
n	54
LS mean (SE)	85.80 (2.26)
95% CI of LS mean	(81.26, 90.35)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	6.69 (2.26)
95% CI of LS mean	(2.14, 11.23)
Week 24	
n	54
Mean (SD)	82.51 (19.85)
Absolute Change at Week 24	
n	54
Mean (SD)	3.40 (20.77)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	82.51 (2.12)
95% CI of LS mean	(78.26, 86.76)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	3.40 (2.12)
95% CI of LS mean	(-0.85, 7.64)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	5.04 (1.90)
95% CI of LS mean	(1.23, 8.85)
P-value	0.0106

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	82.51 (17.48)
Week 4 (MMRM)	
n	54
LS mean (SE)	83.13 (2.31)
95% CI of LS mean	(78.50, 87.76)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	0.62 (2.31)
95% CI of LS mean	(-4.01, 5.25)
Week 8 (MMRM)	
n	54
LS mean (SE)	82.51 (1.87)
95% CI of LS mean	(78.75, 86.27)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	0.00 (1.87)
95% CI of LS mean	(-3.76, 3.76)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	84.69 (1.89)
95% CI of LS mean	(80.90, 88.48)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	2.18 (1.89)
95% CI of LS mean	(-1.61, 5.97)
Week 16 (MMRM)	
n	54
LS mean (SE)	85.60 (1.61)
95% CI of LS mean	(82.37, 88.83)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	3.09 (1.61)
95% CI of LS mean	(-0.14, 6.32)
Week 24	
n	54
Mean (SD)	81.48 (14.80)
Absolute Change at Week 24	
n	54
Mean (SD)	-1.03 (17.03)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	81.48 (1.80)
95% CI of LS mean	(77.86, 85.10)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	-1.03 (1.80)
95% CI of LS mean	(-4.65, 2.59)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	1.03 (1.47)
95% CI of LS mean	(-1.92, 3.98)
P-value	0.4872

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	76.54 (26.01)
Week 4 (MMRM)	
n	54
LS mean (SE)	75.62 (2.29)
95% CI of LS mean	(71.02, 80.21)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	-0.93 (2.29)
95% CI of LS mean	(-5.52, 3.67)
Week 8 (MMRM)	
n	54
LS mean (SE)	75.31 (2.66)
95% CI of LS mean	(69.97, 80.65)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	-1.23 (2.66)
95% CI of LS mean	(-6.57, 4.10)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	75.56 (2.46)
95% CI of LS mean	(70.63, 80.49)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	-0.98 (2.46)
95% CI of LS mean	(-5.91, 3.95)
Week 16 (MMRM)	
n	54
LS mean (SE)	78.70 (1.83)
95% CI of LS mean	(75.04, 82.37)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	2.16 (1.83)
95% CI of LS mean	(-1.50, 5.82)
Week 24	
n	54
Mean (SD)	80.25 (22.68)
Absolute Change at Week 24	
n	54
Mean (SD)	3.70 (19.60)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	80.25 (2.26)
95% CI of LS mean	(75.71, 84.79)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	3.70 (2.26)
95% CI of LS mean	(-0.83, 8.24)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	2.93 (1.75)
95% CI of LS mean	(-0.57, 6.43)
P-value	0.0990

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	85.09 (14.10)
Week 4 (MMRM)	
n	54
LS mean (SE)	85.80 (1.22)
95% CI of LS mean	(83.36, 88.24)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	0.71 (1.22)
95% CI of LS mean	(-1.73, 3.15)
Week 8 (MMRM)	
n	54
LS mean (SE)	85.25 (1.22)
95% CI of LS mean	(82.81, 87.69)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	0.15 (1.22)
95% CI of LS mean	(-2.29, 2.60)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	88.38 (1.32)
95% CI of LS mean	(85.72, 91.03)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	3.28 (1.32)
95% CI of LS mean	(0.63, 5.94)
Week 16 (MMRM)	
n	54
LS mean (SE)	88.64 (1.31)
95% CI of LS mean	(86.01, 91.27)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	3.55 (1.31)
95% CI of LS mean	(0.92, 6.18)
Week 24	
n	54
Mean (SD)	88.64 (10.33)
Absolute Change at Week 24	
n	54
Mean (SD)	3.55 (12.33)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	88.64 (1.23)
95% CI of LS mean	(86.18, 91.11)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	3.55 (1.23)
95% CI of LS mean	(1.08, 6.02)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	3.55 (0.90)
95% CI of LS mean	(1.74, 5.36)
P-value	0.0003

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	86.63 (13.54)
Week 4 (MMRM)	
n	54
LS mean (SE)	83.33 (1.87)
95% CI of LS mean	(79.59, 87.08)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	-3.29 (1.87)
95% CI of LS mean	(-7.04, 0.45)
Week 8 (MMRM)	
n	54
LS mean (SE)	87.45 (1.50)
95% CI of LS mean	(84.44, 90.46)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	0.82 (1.50)
95% CI of LS mean	(-2.19, 3.83)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	87.00 (1.75)
95% CI of LS mean	(83.50, 90.50)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	0.37 (1.75)
95% CI of LS mean	(-3.13, 3.88)
Week 16 (MMRM)	
n	54
LS mean (SE)	89.30 (1.37)
95% CI of LS mean	(86.55, 92.05)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	2.67 (1.37)
95% CI of LS mean	(-0.08, 5.43)
Week 24	
n	54
Mean (SD)	87.04 (17.77)
Absolute Change at Week 24	
n	54
Mean (SD)	0.41 (18.31)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	87.04 (2.30)
95% CI of LS mean	(82.43, 91.65)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	0.41 (2.30)
95% CI of LS mean	(-4.20, 5.02)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	1.54 (1.50)
95% CI of LS mean	(-1.47, 4.56)
P-value	0.3089

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	90.66 (15.03)
Week 4 (MMRM)	
n	54
LS mean (SE)	91.13 (1.44)
95% CI of LS mean	(88.24, 94.02)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	0.46 (1.44)
95% CI of LS mean	(-2.43, 3.35)
Week 8 (MMRM)	
n	54
LS mean (SE)	90.60 (1.35)
95% CI of LS mean	(87.89, 93.30)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	-0.07 (1.35)
95% CI of LS mean	(-2.77, 2.64)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	94.03 (1.06)
95% CI of LS mean	(91.90, 96.16)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	3.37 (1.06)
95% CI of LS mean	(1.24, 5.49)
Week 16 (MMRM)	
n	54
LS mean (SE)	94.52 (1.35)
95% CI of LS mean	(91.80, 97.25)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	3.86 (1.35)
95% CI of LS mean	(1.13, 6.58)
Week 24	
n	54
Mean (SD)	91.59 (14.96)
Absolute Change at Week 24	
n	54
Mean (SD)	0.93 (12.00)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	91.59 (1.54)
95% CI of LS mean	(88.49, 94.69)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	0.93 (1.54)
95% CI of LS mean	(-2.17, 4.02)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	2.39 (1.02)
95% CI of LS mean	(0.34, 4.44)
P-value	0.0231

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	78.24 (18.34)
Week 4 (MMRM)	
n	54
LS mean (SE)	82.87 (1.79)
95% CI of LS mean	(79.28, 86.46)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	4.63 (1.79)
95% CI of LS mean	(1.04, 8.22)
Week 8 (MMRM)	
n	54
LS mean (SE)	81.64 (2.03)
95% CI of LS mean	(77.56, 85.71)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	3.40 (2.03)
95% CI of LS mean	(-0.68, 7.47)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	84.91 (1.65)
95% CI of LS mean	(81.60, 88.22)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	6.67 (1.65)
95% CI of LS mean	(3.36, 9.98)
Week 16 (MMRM)	
n	54
LS mean (SE)	83.80 (2.02)
95% CI of LS mean	(79.74, 87.85)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	5.56 (2.02)
95% CI of LS mean	(1.50, 9.61)
Week 24	
n	54
Mean (SD)	81.79 (16.27)
Absolute Change at Week 24	
n	54
Mean (SD)	3.55 (14.53)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	81.79 (1.69)
95% CI of LS mean	(78.40, 85.18)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	3.55 (1.69)
95% CI of LS mean	(0.16, 6.93)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	4.55 (1.54)
95% CI of LS mean	(1.47, 7.64)
P-value	0.0046

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	70.37 (20.13)
Week 4 (MMRM)	
n	54
LS mean (SE)	78.19 (1.67)
95% CI of LS mean	(74.84, 81.53)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	7.82 (1.67)
95% CI of LS mean	(4.47, 11.16)
Week 8 (MMRM)	
n	54
LS mean (SE)	79.42 (2.56)
95% CI of LS mean	(74.29, 84.56)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	9.05 (2.56)
95% CI of LS mean	(3.92, 14.19)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	77.57 (2.52)
95% CI of LS mean	(72.52, 82.61)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	7.20 (2.52)
95% CI of LS mean	(2.15, 12.24)
Week 16 (MMRM)	
n	54
LS mean (SE)	78.19 (1.99)
95% CI of LS mean	(74.20, 82.18)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	7.82 (1.99)
95% CI of LS mean	(3.83, 11.81)
Week 24	
n	54
Mean (SD)	80.45 (19.05)
Absolute Change at Week 24	
n	54
Mean (SD)	10.08 (19.46)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	80.45 (2.32)
95% CI of LS mean	(75.79, 85.11)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	10.08 (2.32)
95% CI of LS mean	(5.42, 14.74)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	8.95 (1.88)
95% CI of LS mean	(5.18, 12.72)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	75.43 (12.27)
Week 4 (MMRM)	
n	54
LS mean (SE)	73.09 (1.68)
95% CI of LS mean	(69.73, 76.45)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	-2.35 (1.68)
95% CI of LS mean	(-5.71, 1.02)
Week 8 (MMRM)	
n	54
LS mean (SE)	73.21 (1.35)
95% CI of LS mean	(70.51, 75.91)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	-2.22 (1.35)
95% CI of LS mean	(-4.93, 0.48)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	76.36 (1.43)
95% CI of LS mean	(73.48, 79.24)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	0.93 (1.43)
95% CI of LS mean	(-1.95, 3.81)
Week 16 (MMRM)	
n	54
LS mean (SE)	77.41 (1.35)
95% CI of LS mean	(74.71, 80.11)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	1.98 (1.35)
95% CI of LS mean	(-0.73, 4.68)
Week 24	
n	54
Mean (SD)	74.81 (13.56)
Absolute Change at Week 24	
n	54
Mean (SD)	-0.62 (14.72)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	74.81 (1.75)
95% CI of LS mean	(71.30, 78.33)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	-0.62 (1.75)
95% CI of LS mean	(-4.13, 2.89)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	0.68 (1.28)
95% CI of LS mean	(-1.89, 3.24)
P-value	0.5975

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	71.60 (35.71)
Week 4 (MMRM)	
n	54
LS mean (SE)	70.37 (3.65)
95% CI of LS mean	(63.05, 77.69)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	-1.23 (3.65)
95% CI of LS mean	(-8.55, 6.08)
Week 8 (MMRM)	
n	54
LS mean (SE)	77.16 (3.19)
95% CI of LS mean	(70.76, 83.56)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	5.56 (3.19)
95% CI of LS mean	(-0.84, 11.95)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	75.26 (3.10)
95% CI of LS mean	(69.04, 81.48)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	3.65 (3.10)
95% CI of LS mean	(-2.57, 9.88)
Week 16 (MMRM)	
n	54
LS mean (SE)	77.78 (2.98)
95% CI of LS mean	(71.79, 83.76)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	6.17 (2.98)
95% CI of LS mean	(0.19, 12.16)
Week 24	
n	54
Mean (SD)	76.54 (30.80)
Absolute Change at Week 24	
n	54
Mean (SD)	4.94 (30.65)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	76.54 (3.43)
95% CI of LS mean	(69.66, 83.42)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	4.94 (3.43)
95% CI of LS mean	(-1.94, 11.82)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	5.56 (2.76)
95% CI of LS mean	(0.02, 11.09)
P-value	0.0493

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.13
Study VX21-121-105: Summary of Pulmonary Exacerbations through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Total number of days (years) of the PEx analysis period	9148 (27.2)
Pulmonary exacerbations	
Number of subjects with events, n (%)	4 (7.41)
Total number of events	4
Observed event rate per year	0.15
Pulmonary exacerbations requiring hospitalization	
Number of subjects with events, n (%)	1 (1.85)
Total number of events	1
Observed event rate per year	0.04
Pulmonary exacerbations requiring IV antibiotic therapy	
Number of subjects with events, n (%)	1 (1.85)
Total number of events	1
Observed event rate per year	0.04
Pulmonary exacerbations requiring hospitalization or IV antibiotic therapy	
Number of subjects with events, n (%)	1 (1.85)
Total number of events	1
Observed event rate per year	0.04

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 2.2.1.14.1
Study VX21-121-105: Time-to-First Pulmonary Exacerbation through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Any Pulmonary Exacerbation	
Overall	
Subjects with Events	4 (7.41)
Subjects Censored	50 (92.59)
Event-free time (weeks)	
75 percent subjects	-
50 percent subjects (Median)	-
25 percent subjects	-

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.1.15.1
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization	
Overall	
Subjects with Events	1 (1.85)
Subjects Censored	53 (98.15)
Event-free time (weeks)	
75 percent subjects	-
50 percent subjects (Median)	-
25 percent subjects	-

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation requiring hospitalization during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.1.16.1
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics	
Overall	
Subjects with Events	1 (1.85)
Subjects Censored	53 (98.15)
Event-free time (weeks)	
75 percent subjects	-
50 percent subjects (Median)	-
25 percent subjects	-

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation requiring IV antibiotics during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.1.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.4166
Region (North America vs. Rest of the World)	0.7840
LCI$_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline ppFEV$_1$ as covariate.
- N/C: model does not converge.

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Table 2.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	100.32 (10.87)
Week 24	
n	25
Mean (SD)	100.13 (12.23)
Absolute Change at Week 24	
n	25
Mean (SD)	-0.55 (10.22)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	0.31 (2.01)
95% CI of LS mean	(-3.82, 4.44)
P-value	0.8786

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline ppFEV$_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	103.96 (10.14)
Week 24	
n	25
Mean (SD)	102.00 (11.00)
Absolute Change at Week 24	
n	24
Mean (SD)	-3.16 (7.31)
Absolute Change through Week 24 (MMRM)	
n	25
LS mean (SE)	-2.20 (1.02)
95% CI of LS mean	(-4.31, -0.10)
P-value	0.0410

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	100.90 (10.83)
Week 24	
n	34
Mean (SD)	99.65 (12.11)
Absolute Change at Week 24	
n	34
Mean (SD)	-1.55 (5.64)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	-0.21 (0.97)
95% CI of LS mean	(-2.18, 1.76)
P-value	0.8278

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	17
Mean (SD)	104.66 (9.85)
Week 24	
n	16
Mean (SD)	104.07 (9.96)
Absolute Change at Week 24	
n	15
Mean (SD)	-2.47 (14.04)
Absolute Change through Week 24 (MMRM)	
n	16
LS mean (SE)	-2.48 (3.60)
95% CI of LS mean	(-10.29, 5.32)
P-value	0.5028

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline ppFEV$_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA
	N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.2.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0484
Region (North America vs. Rest of the World)	0.5146
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effect and baseline BMI as covariate.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	17.26 (2.44)
Week 24	
n	27
Mean (SD)	17.38 (2.77)
Absolute Change at Week 24	
n	27
Mean (SD)	0.12 (0.67)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	0.12 (0.12)
95% CI of LS mean	(-0.14, 0.37)
P-value	0.3559

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	16.29 (1.70)
Week 24	
n	27
Mean (SD)	16.65 (2.08)
Absolute Change at Week 24	
n	27
Mean (SD)	0.37 (0.86)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	0.37 (0.16)
95% CI of LS mean	(0.03, 0.70)
P-value	0.0321

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	17.16 (2.03)
Week 24	
n	36
Mean (SD)	17.57 (2.36)
Absolute Change at Week 24	
n	36
Mean (SD)	0.41 (0.87)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	0.41 (0.14)
95% CI of LS mean	(0.12, 0.70)
P-value	0.0077

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	16.01 (2.21)
Week 24	
n	18
Mean (SD)	15.92 (2.32)
Absolute Change at Week 24	
n	18
Mean (SD)	-0.09 (0.35)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-0.09 (0.08)
95% CI of LS mean	(-0.26, 0.09)
P-value	0.3027

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA
	N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0363
Region (North America vs. Rest of the World)	0.0822
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effect and baseline BMI z-score as covariate.
- N/C: model does not converge.

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Table 2.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	0.28 (0.87)
Week 24	
n	27
Mean (SD)	0.18 (0.95)
Absolute Change at Week 24	
n	27
Mean (SD)	-0.09 (0.22)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	-0.09 (0.04)
95% CI of LS mean	(-0.18, -0.01)
P-value	0.0342

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	-0.14 (0.80)
Week 24	
n	27
Mean (SD)	-0.11 (0.91)
Absolute Change at Week 24	
n	27
Mean (SD)	0.03 (0.37)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	0.03 (0.07)
95% CI of LS mean	(-0.12, 0.17)
P-value	0.7181

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	0.22 (0.73)
Week 24	
n	36
Mean (SD)	0.25 (0.78)
Absolute Change at Week 24	
n	36
Mean (SD)	0.03 (0.33)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	0.03 (0.06)
95% CI of LS mean	(-0.08, 0.15)
P-value	0.5607

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	-0.23 (1.02)
Week 24	
n	18
Mean (SD)	-0.40 (1.08)
Absolute Change at Week 24	
n	18
Mean (SD)	-0.17 (0.20)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-0.17 (0.05)
95% CI of LS mean	(-0.26, -0.07)
P-value	0.0022

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

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Table 2.2.2.4.1.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.9397
Region (North America vs. Rest of the World)	0.1599
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effect and baseline sweat chloride as covariate.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	36.28 (22.93)
Week 24	
n	26
Mean (SD)	29.06 (15.81)
Absolute Change at Week 24	
n	26
Mean (SD)	-7.58 (16.99)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	-8.28 (2.64)
95% CI of LS mean	(-13.75, -2.80)
P-value	0.0047

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	34.17 (16.27)
Week 24	
n	26
Mean (SD)	26.69 (10.61)
Absolute Change at Week 24	
n	26
Mean (SD)	-7.48 (13.40)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	-7.52 (1.29)
95% CI of LS mean	(-10.18, -4.87)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	37.40 (22.45)
Week 24	
n	35
Mean (SD)	30.04 (15.23)
Absolute Change at Week 24	
n	35
Mean (SD)	-7.46 (16.92)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	-8.25 (2.02)
95% CI of LS mean	(-12.37, -4.13)
P-value	0.0003

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	30.86 (12.05)
Week 24	
n	17
Mean (SD)	23.41 (6.79)
Absolute Change at Week 24	
n	17
Mean (SD)	-7.68 (11.12)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-7.21 (1.30)
95% CI of LS mean	(-9.96, -4.45)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.4.2.1
Study VX21-121-105: Subgroup Factor Test for
Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.5525
Region (North America vs. Rest of the World)	>0.9999
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Chi-square test.

Table 2.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Non-missing value at Week 24, N1	26
Number of subjects with missing value at Week 24	1
SwCl <60 mmol/L at Week 24, n (%)	25 (92.59)
95% CI for the proportion	(75.71, 99.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 2.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Non-missing value at Week 24, N1	26
Number of subjects with missing value at Week 24	1
SwCl <60 mmol/L at Week 24, n (%)	26 (96.30)
95% CI for the proportion	(81.03, 99.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 2.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Non-missing value at Week 24, N1	35
Number of subjects with missing value at Week 24	1
SwCl <60 mmol/L at Week 24, n (%)	34 (94.44)
95% CI for the proportion	(81.34, 99.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 2.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Non-missing value at Week 24, N1	17
Number of subjects with missing value at Week 24	1
SwCl <60 mmol/L at Week 24, n (%)	17 (94.44)
95% CI for the proportion	(72.71, 99.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 2.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 2.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 2.2.2.4.3.1
Study VX21-121-105: Subgroup Factor Test for
Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.7801
Region (North America vs. Rest of the World)	0.2363
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Chi-square test.

Table 2.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Non-missing value at Week 24, N1	26
Number of subjects with missing value at Week 24	1
SwCl <30 mmol/L at Week 24, n (%)	16 (59.26)
95% CI for the proportion	(38.80, 77.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 2.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Non-missing value at Week 24, N1	26
Number of subjects with missing value at Week 24	1
SwCl <30 mmol/L at Week 24, n (%)	17 (62.96)
95% CI for the proportion	(42.37, 80.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 2.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Non-missing value at Week 24, N1	35
Number of subjects with missing value at Week 24	1
SwCl <30 mmol/L at Week 24, n (%)	20 (55.56)
95% CI for the proportion	(38.10, 72.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 2.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Non-missing value at Week 24, N1	17
Number of subjects with missing value at Week 24	1
SwCl <30 mmol/L at Week 24, n (%)	13 (72.22)
95% CI for the proportion	(46.52, 90.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 2.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 2.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 2.2.2.5.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.1199
Region (North America vs. Rest of the World)	0.5170
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effect and baseline weight as covariate.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	30.81 (9.08)
Week 24	
n	27
Mean (SD)	32.31 (10.02)
Absolute Change at Week 24	
n	27
Mean (SD)	1.50 (1.63)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	1.50 (0.29)
95% CI of LS mean	(0.90, 2.09)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	29.14 (7.36)
Week 24	
n	27
Mean (SD)	31.05 (8.01)
Absolute Change at Week 24	
n	27
Mean (SD)	1.91 (1.59)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	1.91 (0.30)
95% CI of LS mean	(1.28, 2.53)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	31.21 (8.44)
Week 24	
n	36
Mean (SD)	33.12 (9.19)
Absolute Change at Week 24	
n	36
Mean (SD)	1.91 (1.82)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	1.91 (0.29)
95% CI of LS mean	(1.32, 2.51)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	27.52 (7.39)
Week 24	
n	18
Mean (SD)	28.80 (8.12)
Absolute Change at Week 24	
n	18
Mean (SD)	1.28 (1.00)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	1.28 (0.19)
95% CI of LS mean	(0.86, 1.70)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

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Table 2.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

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Table 2.2.2.6.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0354
Region (North America vs. Rest of the World)	0.5321
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effect and baseline weight z-score as covariate.
- N/C: model does not converge.

Table 2.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	0.14 (0.93)
Week 24	
n	27
Mean (SD)	0.08 (1.01)
Absolute Change at Week 24	
n	27
Mean (SD)	-0.06 (0.19)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	-0.06 (0.04)
95% CI of LS mean	(-0.13, 0.02)
P-value	0.1215

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	-0.13 (0.89)
Week 24	
n	27
Mean (SD)	-0.09 (0.92)
Absolute Change at Week 24	
n	27
Mean (SD)	0.04 (0.25)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	0.04 (0.05)
95% CI of LS mean	(-0.06, 0.14)
P-value	0.4684

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	0.06 (0.87)
Week 24	
n	36
Mean (SD)	0.08 (0.92)
Absolute Change at Week 24	
n	36
Mean (SD)	0.02 (0.26)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	0.02 (0.04)
95% CI of LS mean	(-0.07, 0.11)
P-value	0.6759

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	-0.10 (1.00)
Week 24	
n	18
Mean (SD)	-0.17 (1.04)
Absolute Change at Week 24	
n	18
Mean (SD)	-0.07 (0.14)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-0.07 (0.03)
95% CI of LS mean	(-0.14, 0.00)
P-value	0.0566

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

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Table 2.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.7.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.2332
Region (North America vs. Rest of the World)	0.2349
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effect and baseline height as covariate.
- N/C: model does not converge.

Table 2.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	132.11 (10.56)
Week 24	
n	27
Mean (SD)	134.71 (10.61)
Absolute Change at Week 24	
n	27
Mean (SD)	2.60 (1.01)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	2.60 (0.20)
95% CI of LS mean	(2.20, 3.01)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	132.62 (11.68)
Week 24	
n	27
Mean (SD)	135.40 (12.03)
Absolute Change at Week 24	
n	27
Mean (SD)	2.78 (1.15)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	2.78 (0.22)
95% CI of LS mean	(2.33, 3.22)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	133.52 (11.51)
Week 24	
n	36
Mean (SD)	135.94 (11.67)
Absolute Change at Week 24	
n	36
Mean (SD)	2.42 (1.05)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	2.42 (0.17)
95% CI of LS mean	(2.07, 2.77)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	130.05 (9.91)
Week 24	
n	18
Mean (SD)	133.28 (10.40)
Absolute Change at Week 24	
n	18
Mean (SD)	3.23 (0.94)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	3.23 (0.22)
95% CI of LS mean	(2.75, 3.71)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

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Table 2.2.2.8.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.2884
Region (North America vs. Rest of the World)	0.3205
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effect and baseline height z-score as covariate.
- N/C: model does not converge.

Table 2.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	-0.08 (0.94)
Week 24	
n	27
Mean (SD)	-0.07 (0.93)
Absolute Change at Week 24	
n	27
Mean (SD)	0.01 (0.18)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	0.01 (0.03)
95% CI of LS mean	(-0.06, 0.08)
P-value	0.7602

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	0.05 (0.99)
Week 24	
n	27
Mean (SD)	0.05 (1.05)
Absolute Change at Week 24	
n	27
Mean (SD)	-0.01 (0.19)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	-0.01 (0.04)
95% CI of LS mean	(-0.08, 0.07)
P-value	0.8675

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	-0.07 (1.02)
Week 24	
n	36
Mean (SD)	-0.10 (1.05)
Absolute Change at Week 24	
n	36
Mean (SD)	-0.03 (0.18)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	-0.03 (0.03)
95% CI of LS mean	(-0.09, 0.03)
P-value	0.3505

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	0.10 (0.84)
Week 24	
n	18
Mean (SD)	0.17 (0.84)
Absolute Change at Week 24	
n	18
Mean (SD)	0.07 (0.16)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	0.07 (0.04)
95% CI of LS mean	(-0.02, 0.15)
P-value	0.1099

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA
	N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.9.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0004
Region (North America vs. Rest of the World)	0.8921
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline $LCI_{2.5}$ as covariate.
- N/C: model does not converge.

Table 2.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	25
Mean (SD)	6.47 (0.46)
Week 24	
n	21
Mean (SD)	6.31 (0.32)
Absolute Change at Week 24	
n	20
Mean (SD)	-0.28 (0.51)
Absolute Change through Week 24 (MMRM)	
n	20
LS mean (SE)	-0.23 (0.06)
95% CI of LS mean	(-0.36, -0.11)
P-value	0.0013

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 2.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	6.55 (0.60)
Week 24	
n	23
Mean (SD)	6.59 (0.64)
Absolute Change at Week 24	
n	22
Mean (SD)	-0.01 (0.50)
Absolute Change through Week 24 (MMRM)	
n	22
LS mean (SE)	0.08 (0.08)
95% CI of LS mean	(-0.09, 0.26)
P-value	0.3289

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 2.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	33
Mean (SD)	6.50 (0.54)
Week 24	
n	29
Mean (SD)	6.48 (0.54)
Absolute Change at Week 24	
n	27
Mean (SD)	-0.13 (0.52)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	-0.07 (0.07)
95% CI of LS mean	(-0.22, 0.07)
P-value	0.3069

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 2.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	6.52 (0.52)
Week 24	
n	15
Mean (SD)	6.42 (0.52)
Absolute Change at Week 24	
n	15
Mean (SD)	-0.16 (0.54)
Absolute Change through Week 24 (MMRM)	
n	15
LS mean (SE)	-0.05 (0.11)
95% CI of LS mean	(-0.28, 0.18)
P-value	0.6513

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 2.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 2.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA
	N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.3174
Region (North America vs. Rest of the World)	0.1710
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Respiratory domain score as covariate.
- N/C: model does not converge.

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Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	82.37 (16.55)
Week 4 (MMRM)	
n	26
LS mean (SE)	82.37 (2.05)
95% CI of LS mean	(78.13, 86.62)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	0.00 (2.05)
95% CI of LS mean	(-4.25, 4.25)
Week 8 (MMRM)	
n	26
LS mean (SE)	83.65 (2.78)
95% CI of LS mean	(77.92, 89.39)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	1.28 (2.78)
95% CI of LS mean	(-4.45, 7.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	25
LS mean (SE)	87.91 (2.26)
95% CI of LS mean	(83.26, 92.57)
Absolute Change at Week 12 (MMRM)	
n	25
LS mean (SE)	5.54 (2.26)
95% CI of LS mean	(0.88, 10.20)
Week 16 (MMRM)	
n	26
LS mean (SE)	88.78 (2.52)
95% CI of LS mean	(83.59, 93.97)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	6.41 (2.52)
95% CI of LS mean	(1.22, 11.60)
Week 24	
n	27
Mean (SD)	84.26 (17.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	2.56 (20.11)
Week 24 (MMRM)	
n	27
LS mean (SE)	84.94 (3.42)
95% CI of LS mean	(77.88, 91.99)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	2.56 (3.42)
95% CI of LS mean	(-4.49, 9.62)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	4.49 (2.38)
95% CI of LS mean	(-0.44, 9.42)
P-value	0.0725

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	82.69 (20.13)
Week 4 (MMRM)	
n	26
LS mean (SE)	84.29 (3.74)
95% CI of LS mean	(76.59, 92.00)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	1.60 (3.74)
95% CI of LS mean	(-6.11, 9.31)
Week 8 (MMRM)	
n	26
LS mean (SE)	86.54 (3.65)
95% CI of LS mean	(79.01, 94.07)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	3.85 (3.65)
95% CI of LS mean	(-3.68, 11.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	91.67 (2.16)
95% CI of LS mean	(87.22, 96.11)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	8.97 (2.16)
95% CI of LS mean	(4.53, 13.42)
Week 16 (MMRM)	
n	26
LS mean (SE)	92.31 (2.24)
95% CI of LS mean	(87.70, 96.92)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	9.62 (2.24)
95% CI of LS mean	(5.01, 14.23)
Week 24	
n	27
Mean (SD)	84.26 (17.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	3.21 (22.86)
Week 24 (MMRM)	
n	27
LS mean (SE)	85.90 (3.05)
95% CI of LS mean	(79.61, 92.18)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	3.21 (3.05)
95% CI of LS mean	(-3.08, 9.49)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	6.41 (2.25)
95% CI of LS mean	(1.78, 11.04)
P-value	0.0087

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	81.25 (19.25)
Week 4 (MMRM)	
n	36
LS mean (SE)	79.86 (2.91)
95% CI of LS mean	(73.95, 85.78)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	-1.39 (2.91)
95% CI of LS mean	(-7.30, 4.53)
Week 8 (MMRM)	
n	36
LS mean (SE)	83.33 (2.86)
95% CI of LS mean	(77.53, 89.14)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	2.08 (2.86)
95% CI of LS mean	(-3.72, 7.89)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	88.89 (2.08)
95% CI of LS mean	(84.67, 93.11)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	7.64 (2.08)
95% CI of LS mean	(3.42, 11.86)
Week 16 (MMRM)	
n	36
LS mean (SE)	90.05 (2.04)
95% CI of LS mean	(85.90, 94.20)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	8.80 (2.04)
95% CI of LS mean	(4.65, 12.95)
Week 24	
n	36
Mean (SD)	83.10 (16.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	1.85 (21.56)
Week 24 (MMRM)	
n	36
LS mean (SE)	83.10 (2.67)
95% CI of LS mean	(77.69, 88.52)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	1.85 (2.67)
95% CI of LS mean	(-3.56, 7.27)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	5.32 (1.95)
95% CI of LS mean	(1.36, 9.29)
P-value	0.0100

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	16
Mean (SD)	85.42 (15.96)
Week 4 (MMRM)	
n	16
LS mean (SE)	91.15 (3.14)
95% CI of LS mean	(84.39, 97.91)
Absolute Change at Week 4 (MMRM)	
n	16
LS mean (SE)	5.73 (3.14)
95% CI of LS mean	(-1.03, 12.49)
Week 8 (MMRM)	
n	16
LS mean (SE)	89.06 (2.92)
95% CI of LS mean	(82.65, 95.48)
Absolute Change at Week 8 (MMRM)	
n	16
LS mean (SE)	3.65 (2.92)
95% CI of LS mean	(-2.77, 10.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	15
LS mean (SE)	92.28 (3.37)
95% CI of LS mean	(85.02, 99.55)
Absolute Change at Week 12 (MMRM)	
n	15
LS mean (SE)	6.86 (3.37)
95% CI of LS mean	(-0.40, 14.13)
Week 16 (MMRM)	
n	16
LS mean (SE)	91.67 (4.08)
95% CI of LS mean	(82.81, 100.52)
Absolute Change at Week 16 (MMRM)	
n	16
LS mean (SE)	6.25 (4.08)
95% CI of LS mean	(-2.61, 15.11)
Week 24	
n	18
Mean (SD)	86.57 (18.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	16
Mean (SD)	5.21 (21.27)
Week 24 (MMRM)	
n	18
LS mean (SE)	90.63 (4.33)
95% CI of LS mean	(81.27, 99.98)
Absolute Change at Week 24 (MMRM)	
n	16
LS mean (SE)	5.21 (4.33)
95% CI of LS mean	(-4.14, 14.56)
Absolute Change through Week 24 (MMRM)	
n	16
LS mean (SE)	5.73 (3.59)
95% CI of LS mean	(-2.17, 13.63)
P-value	0.1389

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.6496
Region (North America vs. Rest of the World)	0.1402
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Respiratory domain score as covariate.
- N/C: model does not converge.

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Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	84.77 (16.20)
Week 4 (MMRM)	
n	27
LS mean (SE)	83.54 (3.18)
95% CI of LS mean	(77.01, 90.07)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-1.23 (3.18)
95% CI of LS mean	(-7.77, 5.30)
Week 8 (MMRM)	
n	27
LS mean (SE)	85.80 (2.91)
95% CI of LS mean	(79.82, 91.79)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	1.03 (2.91)
95% CI of LS mean	(-4.96, 7.02)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	92.33 (1.74)
95% CI of LS mean	(88.75, 95.91)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	7.56 (1.74)
95% CI of LS mean	(3.98, 11.14)
Week 16 (MMRM)	
n	27
LS mean (SE)	88.19 (3.28)
95% CI of LS mean	(81.44, 94.94)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	3.42 (3.28)
95% CI of LS mean	(-3.33, 10.16)
Week 24	
n	27
Mean (SD)	87.65 (15.59)
Absolute Change at Week 24	
n	27
Mean (SD)	2.88 (18.39)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 24 (MMRM)	
n	27
LS mean (SE)	87.65 (2.85)
95% CI of LS mean	(81.80, 93.51)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	2.88 (2.85)
95% CI of LS mean	(-2.97, 8.74)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	3.15 (2.47)
95% CI of LS mean	(-1.93, 8.22)
P-value	0.2135

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	86.26 (19.36)
Week 4 (MMRM)	
n	27
LS mean (SE)	86.63 (3.82)
95% CI of LS mean	(78.77, 94.49)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	0.37 (3.82)
95% CI of LS mean	(-7.49, 8.23)
Week 8 (MMRM)	
n	27
LS mean (SE)	87.65 (3.01)
95% CI of LS mean	(81.47, 93.84)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	1.40 (3.01)
95% CI of LS mean	(-4.79, 7.58)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	91.15 (2.90)
95% CI of LS mean	(85.19, 97.12)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	4.90 (2.90)
95% CI of LS mean	(-1.07, 10.86)
Week 16 (MMRM)	
n	27
LS mean (SE)	94.03 (2.00)
95% CI of LS mean	(89.92, 98.15)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	7.78 (2.00)
95% CI of LS mean	(3.66, 11.90)
Week 24	
n	27
Mean (SD)	85.19 (18.87)
Absolute Change at Week 24	
n	27
Mean (SD)	-1.07 (27.02)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 24 (MMRM)	
n	27
LS mean (SE)	85.19 (3.66)
95% CI of LS mean	(77.65, 92.72)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	-1.07 (3.66)
95% CI of LS mean	(-8.61, 6.47)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	3.35 (2.46)
95% CI of LS mean	(-1.70, 8.41)
P-value	0.1839

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	84.29 (19.11)
Week 4 (MMRM)	
n	36
LS mean (SE)	84.26 (2.71)
95% CI of LS mean	(78.77, 89.75)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	-0.03 (2.71)
95% CI of LS mean	(-5.53, 5.46)
Week 8 (MMRM)	
n	36
LS mean (SE)	86.27 (2.39)
95% CI of LS mean	(81.41, 91.13)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	1.98 (2.39)
95% CI of LS mean	(-2.88, 6.84)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	92.90 (2.06)
95% CI of LS mean	(88.72, 97.08)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	8.61 (2.06)
95% CI of LS mean	(4.43, 12.79)
Week 16 (MMRM)	
n	36
LS mean (SE)	93.83 (1.45)
95% CI of LS mean	(90.89, 96.77)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	9.54 (1.45)
95% CI of LS mean	(6.60, 12.48)
Week 24	
n	36
Mean (SD)	87.35 (16.46)
Absolute Change at Week 24	
n	36
Mean (SD)	3.06 (21.17)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 24 (MMRM)	
n	36
LS mean (SE)	87.35 (2.67)
95% CI of LS mean	(81.93, 92.76)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	3.06 (2.67)
95% CI of LS mean	(-2.36, 8.47)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	6.30 (1.61)
95% CI of LS mean	(3.03, 9.57)
P-value	0.0004

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	87.96 (14.67)
Week 4 (MMRM)	
n	18
LS mean (SE)	86.73 (5.60)
95% CI of LS mean	(74.86, 98.60)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	-1.23 (5.60)
95% CI of LS mean	(-13.10, 10.64)
Week 8 (MMRM)	
n	18
LS mean (SE)	87.65 (3.08)
95% CI of LS mean	(81.13, 94.18)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	-0.31 (3.08)
95% CI of LS mean	(-6.84, 6.22)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	89.74 (3.39)
95% CI of LS mean	(82.38, 97.10)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	1.78 (3.39)
95% CI of LS mean	(-5.59, 9.14)
Week 16 (MMRM)	
n	18
LS mean (SE)	85.68 (5.17)
95% CI of LS mean	(74.70, 96.66)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	-2.28 (5.17)
95% CI of LS mean	(-13.26, 8.69)
Week 24	
n	18
Mean (SD)	84.57 (18.92)
Absolute Change at Week 24	
n	18
Mean (SD)	-3.40 (26.34)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 24 (MMRM)	
n	18
LS mean (SE)	84.57 (5.80)
95% CI of LS mean	(72.12, 97.02)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	-3.40 (5.80)
95% CI of LS mean	(-15.84, 9.05)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-2.84 (4.92)
95% CI of LS mean	(-13.40, 7.72)
P-value	0.5729

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Body

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.7671
Region (North America vs. Rest of the World)	0.4673
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Body domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Digestion

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.6414
Region (North America vs. Rest of the World)	0.4330
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Digestion domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Eat

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.3103
Region (North America vs. Rest of the World)	0.3122
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Eat domain score as covariate.
- N/C: model does not converge.

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Table 2.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Emotion

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.9606
Region (North America vs. Rest of the World)	0.1873
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Emotion domain score as covariate.
- N/C: model does not converge.

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Table 2.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Physical

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.5530
Region (North America vs. Rest of the World)	0.1474
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Physical domain score as covariate.
- N/C: model does not converge.

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Table 2.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Social

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.8639
Region (North America vs. Rest of the World)	0.8423
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Social domain score as covariate.
- N/C: model does not converge.

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Table 2.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Treatment Burden

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.7027
Region (North America vs. Rest of the World)	0.0046
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Treatment Burden domain score as covariate.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	81.20 (24.90)
Week 4 (MMRM)	
n	26
LS mean (SE)	85.47 (4.40)
95% CI of LS mean	(76.41, 94.53)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	4.27 (4.40)
95% CI of LS mean	(-4.79, 13.34)
Week 8 (MMRM)	
n	26
LS mean (SE)	88.46 (3.88)
95% CI of LS mean	(80.37, 96.55)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	7.26 (3.88)
95% CI of LS mean	(-0.83, 15.36)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	25
LS mean (SE)	88.27 (2.95)
95% CI of LS mean	(82.11, 94.42)
Absolute Change at Week 12 (MMRM)	
n	25
LS mean (SE)	7.07 (2.95)
95% CI of LS mean	(0.92, 13.22)
Week 16 (MMRM)	
n	26
LS mean (SE)	90.60 (2.60)
95% CI of LS mean	(85.23, 95.97)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	9.40 (2.60)
95% CI of LS mean	(4.03, 14.77)
Week 24	
n	27
Mean (SD)	87.24 (22.79)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	5.56 (30.83)
Week 24 (MMRM)	
n	27
LS mean (SE)	86.75 (4.48)
95% CI of LS mean	(77.51, 95.99)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	5.56 (4.48)
95% CI of LS mean	(-3.68, 14.79)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	7.48 (3.01)
95% CI of LS mean	(1.27, 13.69)
P-value	0.0203

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	76.92 (26.09)
Week 4 (MMRM)	
n	26
LS mean (SE)	78.63 (2.95)
95% CI of LS mean	(72.50, 84.77)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	1.71 (2.95)
95% CI of LS mean	(-4.43, 7.85)
Week 8 (MMRM)	
n	26
LS mean (SE)	84.19 (3.45)
95% CI of LS mean	(77.09, 91.29)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	7.26 (3.45)
95% CI of LS mean	(0.17, 14.36)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	87.18 (3.68)
95% CI of LS mean	(79.58, 94.78)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	10.26 (3.68)
95% CI of LS mean	(2.65, 17.86)
Week 16 (MMRM)	
n	26
LS mean (SE)	88.89 (3.05)
95% CI of LS mean	(82.60, 95.18)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	11.97 (3.05)
95% CI of LS mean	(5.67, 18.26)
Week 24	
n	27
Mean (SD)	83.13 (23.94)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	5.98 (23.98)
Week 24 (MMRM)	
n	27
LS mean (SE)	82.91 (4.01)
95% CI of LS mean	(74.64, 91.17)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	5.98 (4.01)
95% CI of LS mean	(-2.29, 14.25)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	8.97 (3.22)
95% CI of LS mean	(2.33, 15.62)
P-value	0.0102

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	76.23 (26.04)
Week 4 (MMRM)	
n	36
LS mean (SE)	80.86 (3.74)
95% CI of LS mean	(73.27, 88.46)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	4.63 (3.74)
95% CI of LS mean	(-2.96, 12.22)
Week 8 (MMRM)	
n	36
LS mean (SE)	82.72 (3.53)
95% CI of LS mean	(75.54, 89.89)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	6.48 (3.53)
95% CI of LS mean	(-0.69, 13.65)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	88.27 (2.42)
95% CI of LS mean	(83.36, 93.18)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	12.04 (2.42)
95% CI of LS mean	(7.13, 16.95)
Week 16 (MMRM)	
n	36
LS mean (SE)	89.20 (2.74)
95% CI of LS mean	(83.63, 94.76)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	12.96 (2.74)
95% CI of LS mean	(7.40, 18.53)
Week 24	
n	36
Mean (SD)	82.10 (26.73)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	5.86 (30.92)
Week 24 (MMRM)	
n	36
LS mean (SE)	82.10 (4.24)
95% CI of LS mean	(73.48, 90.72)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	5.86 (4.24)
95% CI of LS mean	(-2.75, 14.48)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	9.41 (3.16)
95% CI of LS mean	(2.99, 15.84)
P-value	0.0053

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	16
Mean (SD)	85.42 (23.21)
Week 4 (MMRM)	
n	16
LS mean (SE)	84.72 (3.47)
95% CI of LS mean	(77.26, 92.19)
Absolute Change at Week 4 (MMRM)	
n	16
LS mean (SE)	-0.69 (3.47)
95% CI of LS mean	(-8.16, 6.77)
Week 8 (MMRM)	
n	16
LS mean (SE)	94.44 (1.30)
95% CI of LS mean	(91.63, 97.26)
Absolute Change at Week 8 (MMRM)	
n	16
LS mean (SE)	9.03 (1.30)
95% CI of LS mean	(6.21, 11.84)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	15
LS mean (SE)	86.89 (4.93)
95% CI of LS mean	(76.38, 97.41)
Absolute Change at Week 12 (MMRM)	
n	15
LS mean (SE)	1.48 (4.93)
95% CI of LS mean	(-9.04, 11.99)
Week 16 (MMRM)	
n	16
LS mean (SE)	90.97 (2.39)
95% CI of LS mean	(85.83, 96.11)
Absolute Change at Week 16 (MMRM)	
n	16
LS mean (SE)	5.56 (2.39)
95% CI of LS mean	(0.41, 10.70)
Week 24	
n	18
Mean (SD)	91.36 (12.38)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	16
Mean (SD)	5.56 (17.68)
Week 24 (MMRM)	
n	18
LS mean (SE)	90.97 (2.47)
95% CI of LS mean	(85.71, 96.24)
Absolute Change at Week 24 (MMRM)	
n	16
LS mean (SE)	5.56 (2.47)
95% CI of LS mean	(0.29, 10.82)
Absolute Change through Week 24 (MMRM)	
n	16
LS mean (SE)	5.56 (1.68)
95% CI of LS mean	(1.93, 9.18)
P-value	0.0055

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	25
Mean (SD)	77.33 (23.01)
Week 4 (MMRM)	
n	26
LS mean (SE)	70.67 (5.47)
95% CI of LS mean	(59.36, 81.97)
Absolute Change at Week 4 (MMRM)	
n	25
LS mean (SE)	-6.67 (5.47)
95% CI of LS mean	(-17.97, 4.64)
Week 8 (MMRM)	
n	26
LS mean (SE)	72.00 (5.18)
95% CI of LS mean	(61.31, 82.69)
Absolute Change at Week 8 (MMRM)	
n	25
LS mean (SE)	-5.33 (5.18)
95% CI of LS mean	(-16.02, 5.36)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	25
LS mean (SE)	81.32 (4.38)
95% CI of LS mean	(72.25, 90.38)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	3.98 (4.38)
95% CI of LS mean	(-5.09, 13.05)
Week 16 (MMRM)	
n	26
LS mean (SE)	84.00 (4.13)
95% CI of LS mean	(75.47, 92.53)
Absolute Change at Week 16 (MMRM)	
n	25
LS mean (SE)	6.67 (4.13)
95% CI of LS mean	(-1.87, 15.20)
Week 24	
n	27
Mean (SD)	83.95 (23.33)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	25
Mean (SD)	6.67 (25.46)
Week 24 (MMRM)	
n	27
LS mean (SE)	84.00 (4.48)
95% CI of LS mean	(74.71, 93.29)
Absolute Change at Week 24 (MMRM)	
n	25
LS mean (SE)	6.67 (4.48)
95% CI of LS mean	(-2.62, 15.95)
Absolute Change through Week 24 (MMRM)	
n	25
LS mean (SE)	6.67 (3.85)
95% CI of LS mean	(-1.30, 14.64)
P-value	0.0970

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	80.77 (21.44)
Week 4 (MMRM)	
n	26
LS mean (SE)	73.08 (6.00)
95% CI of LS mean	(60.71, 85.44)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	-7.69 (6.00)
95% CI of LS mean	(-20.06, 4.67)
Week 8 (MMRM)	
n	26
LS mean (SE)	80.77 (4.32)
95% CI of LS mean	(71.86, 89.68)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	0.00 (4.32)
95% CI of LS mean	(-8.91, 8.91)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	76.92 (3.81)
95% CI of LS mean	(69.06, 84.78)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	-3.85 (3.81)
95% CI of LS mean	(-11.71, 4.01)
Week 16 (MMRM)	
n	26
LS mean (SE)	80.77 (4.35)
95% CI of LS mean	(71.78, 89.76)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	0.00 (4.35)
95% CI of LS mean	(-8.99, 8.99)
Week 24	
n	27
Mean (SD)	82.72 (23.33)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	1.28 (25.79)
Week 24 (MMRM)	
n	27
LS mean (SE)	82.05 (4.39)
95% CI of LS mean	(73.01, 91.09)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	1.28 (4.39)
95% CI of LS mean	(-7.76, 10.33)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	0.64 (3.57)
95% CI of LS mean	(-6.71, 7.99)
P-value	0.8588

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	80.56 (23.06)
Week 4 (MMRM)	
n	36
LS mean (SE)	73.15 (5.19)
95% CI of LS mean	(62.61, 83.69)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	-7.41 (5.19)
95% CI of LS mean	(-17.94, 3.13)
Week 8 (MMRM)	
n	36
LS mean (SE)	76.85 (4.18)
95% CI of LS mean	(68.37, 85.33)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	-3.70 (4.18)
95% CI of LS mean	(-12.18, 4.78)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	79.63 (3.58)
95% CI of LS mean	(72.35, 86.91)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	-0.93 (3.58)
95% CI of LS mean	(-8.20, 6.35)
Week 16 (MMRM)	
n	36
LS mean (SE)	78.70 (3.89)
95% CI of LS mean	(70.81, 86.60)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	-1.85 (3.89)
95% CI of LS mean	(-9.74, 6.04)
Week 24	
n	36
Mean (SD)	81.48 (24.49)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	0.93 (24.54)
Week 24 (MMRM)	
n	36
LS mean (SE)	81.48 (3.65)
95% CI of LS mean	(74.07, 88.89)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	0.93 (3.65)
95% CI of LS mean	(-6.48, 8.34)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	-0.46 (3.31)
95% CI of LS mean	(-7.19, 6.26)
P-value	0.8896

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	15
Mean (SD)	75.56 (19.79)
Week 4 (MMRM)	
n	16
LS mean (SE)	68.89 (7.14)
95% CI of LS mean	(53.44, 84.34)
Absolute Change at Week 4 (MMRM)	
n	15
LS mean (SE)	-6.67 (7.14)
95% CI of LS mean	(-22.12, 8.79)
Week 8 (MMRM)	
n	16
LS mean (SE)	75.56 (6.32)
95% CI of LS mean	(61.77, 89.34)
Absolute Change at Week 8 (MMRM)	
n	15
LS mean (SE)	0.00 (6.32)
95% CI of LS mean	(-13.79, 13.79)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	15
LS mean (SE)	76.36 (4.92)
95% CI of LS mean	(65.73, 86.98)
Absolute Change at Week 12 (MMRM)	
n	14
LS mean (SE)	0.80 (4.92)
95% CI of LS mean	(-9.82, 11.42)
Week 16 (MMRM)	
n	16
LS mean (SE)	91.11 (3.86)
95% CI of LS mean	(82.81, 99.41)
Absolute Change at Week 16 (MMRM)	
n	15
LS mean (SE)	15.56 (3.86)
95% CI of LS mean	(7.26, 23.85)
Week 24	
n	18
Mean (SD)	87.04 (20.26)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	15
Mean (SD)	11.11 (27.22)
Week 24 (MMRM)	
n	18
LS mean (SE)	86.67 (5.49)
95% CI of LS mean	(74.88, 98.45)
Absolute Change at Week 24 (MMRM)	
n	15
LS mean (SE)	11.11 (5.49)
95% CI of LS mean	(-0.67, 22.90)
Absolute Change through Week 24 (MMRM)	
n	15
LS mean (SE)	13.33 (3.50)
95% CI of LS mean	(5.78, 20.88)
P-value	0.0021

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	76.07 (24.68)
Week 4 (MMRM)	
n	26
LS mean (SE)	82.48 (2.84)
95% CI of LS mean	(76.61, 88.35)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	6.41 (2.84)
95% CI of LS mean	(0.54, 12.28)
Week 8 (MMRM)	
n	26
LS mean (SE)	76.07 (4.02)
95% CI of LS mean	(67.76, 84.38)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	0.00 (4.02)
95% CI of LS mean	(-8.31, 8.31)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	25
LS mean (SE)	83.34 (4.54)
95% CI of LS mean	(74.00, 92.68)
Absolute Change at Week 12 (MMRM)	
n	25
LS mean (SE)	7.27 (4.54)
95% CI of LS mean	(-2.07, 16.61)
Week 16 (MMRM)	
n	26
LS mean (SE)	83.33 (3.71)
95% CI of LS mean	(75.70, 90.97)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	7.26 (3.71)
95% CI of LS mean	(-0.37, 14.90)
Week 24	
n	27
Mean (SD)	86.83 (20.22)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	10.26 (18.03)
Week 24 (MMRM)	
n	27
LS mean (SE)	86.32 (2.95)
95% CI of LS mean	(80.23, 92.42)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	10.26 (2.95)
95% CI of LS mean	(4.16, 16.35)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	8.76 (2.68)
95% CI of LS mean	(3.24, 14.28)
P-value	0.0032

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	80.34 (19.95)
Week 4 (MMRM)	
n	26
LS mean (SE)	76.07 (4.04)
95% CI of LS mean	(67.75, 84.39)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	-4.27 (4.04)
95% CI of LS mean	(-12.59, 4.04)
Week 8 (MMRM)	
n	26
LS mean (SE)	77.78 (3.16)
95% CI of LS mean	(71.24, 84.32)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	-2.56 (3.16)
95% CI of LS mean	(-9.10, 3.98)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	82.48 (3.03)
95% CI of LS mean	(76.23, 88.73)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	2.14 (3.03)
95% CI of LS mean	(-4.11, 8.38)
Week 16 (MMRM)	
n	26
LS mean (SE)	85.04 (2.93)
95% CI of LS mean	(79.00, 91.08)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	4.70 (2.93)
95% CI of LS mean	(-1.34, 10.74)
Week 24	
n	27
Mean (SD)	88.48 (17.29)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	8.55 (18.94)
Week 24 (MMRM)	
n	27
LS mean (SE)	88.89 (3.03)
95% CI of LS mean	(82.65, 95.13)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	8.55 (3.03)
95% CI of LS mean	(2.31, 14.79)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	6.62 (2.55)
95% CI of LS mean	(1.36, 11.88)
P-value	0.0157

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	76.54 (24.02)
Week 4 (MMRM)	
n	36
LS mean (SE)	78.09 (2.75)
95% CI of LS mean	(72.49, 83.69)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	1.54 (2.75)
95% CI of LS mean	(-4.06, 7.14)
Week 8 (MMRM)	
n	36
LS mean (SE)	77.47 (3.22)
95% CI of LS mean	(70.91, 84.02)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	0.93 (3.22)
95% CI of LS mean	(-5.63, 7.48)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	82.72 (3.47)
95% CI of LS mean	(75.68, 89.75)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	6.17 (3.47)
95% CI of LS mean	(-0.86, 13.21)
Week 16 (MMRM)	
n	36
LS mean (SE)	83.02 (3.23)
95% CI of LS mean	(76.45, 89.60)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	6.48 (3.23)
95% CI of LS mean	(-0.09, 13.05)
Week 24	
n	36
Mean (SD)	88.58 (18.11)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	12.04 (19.22)
Week 24 (MMRM)	
n	36
LS mean (SE)	88.58 (2.43)
95% CI of LS mean	(83.63, 93.53)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	12.04 (2.43)
95% CI of LS mean	(7.09, 16.98)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	9.26 (2.40)
95% CI of LS mean	(4.38, 14.14)
P-value	0.0005

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	16
Mean (SD)	81.94 (18.09)
Week 4 (MMRM)	
n	16
LS mean (SE)	81.94 (5.75)
95% CI of LS mean	(69.67, 94.22)
Absolute Change at Week 4 (MMRM)	
n	16
LS mean (SE)	0.00 (5.75)
95% CI of LS mean	(-12.28, 12.28)
Week 8 (MMRM)	
n	16
LS mean (SE)	75.69 (4.31)
95% CI of LS mean	(66.08, 85.31)
Absolute Change at Week 8 (MMRM)	
n	16
LS mean (SE)	-6.25 (4.31)
95% CI of LS mean	(-15.86, 3.36)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	15
LS mean (SE)	83.02 (4.09)
95% CI of LS mean	(74.24, 91.79)
Absolute Change at Week 12 (MMRM)	
n	15
LS mean (SE)	1.07 (4.09)
95% CI of LS mean	(-7.70, 9.85)
Week 16 (MMRM)	
n	16
LS mean (SE)	86.81 (2.80)
95% CI of LS mean	(80.83, 92.78)
Absolute Change at Week 16 (MMRM)	
n	16
LS mean (SE)	4.86 (2.80)
95% CI of LS mean	(-1.12, 10.84)
Week 24	
n	18
Mean (SD)	85.80 (20.10)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	16
Mean (SD)	3.47 (15.03)
Week 24 (MMRM)	
n	18
LS mean (SE)	85.42 (3.84)
95% CI of LS mean	(77.15, 93.69)
Absolute Change at Week 24 (MMRM)	
n	16
LS mean (SE)	3.47 (3.84)
95% CI of LS mean	(-4.80, 11.74)
Absolute Change through Week 24 (MMRM)	
n	16
LS mean (SE)	4.17 (2.68)
95% CI of LS mean	(-1.64, 9.97)
P-value	0.1449

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	75.96 (13.66)
Week 4 (MMRM)	
n	26
LS mean (SE)	75.16 (2.75)
95% CI of LS mean	(69.49, 80.83)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	-0.80 (2.75)
95% CI of LS mean	(-6.47, 4.87)
Week 8 (MMRM)	
n	26
LS mean (SE)	78.85 (2.52)
95% CI of LS mean	(73.65, 84.05)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	2.88 (2.52)
95% CI of LS mean	(-2.31, 8.08)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	25
LS mean (SE)	80.76 (3.15)
95% CI of LS mean	(74.28, 87.25)
Absolute Change at Week 12 (MMRM)	
n	25
LS mean (SE)	4.80 (3.15)
95% CI of LS mean	(-1.69, 11.28)
Week 16 (MMRM)	
n	26
LS mean (SE)	84.29 (3.16)
95% CI of LS mean	(77.76, 90.82)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	8.33 (3.16)
95% CI of LS mean	(1.80, 14.86)
Week 24	
n	27
Mean (SD)	79.63 (15.86)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	4.49 (12.80)
Week 24 (MMRM)	
n	27
LS mean (SE)	80.45 (2.45)
95% CI of LS mean	(75.38, 85.51)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	4.49 (2.45)
95% CI of LS mean	(-0.58, 9.55)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	6.41 (2.55)
95% CI of LS mean	(1.13, 11.69)
P-value	0.0194

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	70.03 (16.12)
Week 4 (MMRM)	
n	26
LS mean (SE)	71.52 (2.36)
95% CI of LS mean	(66.66, 76.38)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	1.49 (2.36)
95% CI of LS mean	(-3.37, 6.35)
Week 8 (MMRM)	
n	26
LS mean (SE)	72.44 (2.69)
95% CI of LS mean	(66.90, 77.98)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	2.40 (2.69)
95% CI of LS mean	(-3.14, 7.94)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	74.36 (2.24)
95% CI of LS mean	(69.74, 78.98)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	4.33 (2.24)
95% CI of LS mean	(-0.29, 8.95)
Week 16 (MMRM)	
n	26
LS mean (SE)	75.32 (2.35)
95% CI of LS mean	(70.45, 80.19)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	5.29 (2.35)
95% CI of LS mean	(0.42, 10.15)
Week 24	
n	27
Mean (SD)	77.31 (14.45)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	7.53 (12.80)
Week 24 (MMRM)	
n	27
LS mean (SE)	77.56 (2.20)
95% CI of LS mean	(73.04, 82.09)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	7.53 (2.20)
95% CI of LS mean	(3.00, 12.06)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	6.41 (2.01)
95% CI of LS mean	(2.25, 10.57)
P-value	0.0040

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	70.95 (15.12)
Week 4 (MMRM)	
n	36
LS mean (SE)	69.94 (2.33)
95% CI of LS mean	(65.21, 74.67)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	-1.01 (2.33)
95% CI of LS mean	(-5.74, 3.73)
Week 8 (MMRM)	
n	36
LS mean (SE)	73.73 (2.35)
95% CI of LS mean	(68.95, 78.51)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	2.78 (2.35)
95% CI of LS mean	(-2.00, 7.56)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	75.93 (2.29)
95% CI of LS mean	(71.27, 80.58)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	4.98 (2.29)
95% CI of LS mean	(0.32, 9.63)
Week 16 (MMRM)	
n	36
LS mean (SE)	77.89 (2.53)
95% CI of LS mean	(72.76, 83.03)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	6.94 (2.53)
95% CI of LS mean	(1.81, 12.08)
Week 24	
n	36
Mean (SD)	76.85 (15.92)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	5.90 (13.08)
Week 24 (MMRM)	
n	36
LS mean (SE)	76.85 (2.05)
95% CI of LS mean	(72.70, 81.01)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	5.90 (2.05)
95% CI of LS mean	(1.75, 10.06)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	6.42 (2.08)
95% CI of LS mean	(2.20, 10.65)
P-value	0.0040

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	16
Mean (SD)	77.60 (14.42)
Week 4 (MMRM)	
n	16
LS mean (SE)	80.99 (2.78)
95% CI of LS mean	(75.01, 86.97)
Absolute Change at Week 4 (MMRM)	
n	16
LS mean (SE)	3.39 (2.78)
95% CI of LS mean	(-2.59, 9.36)
Week 8 (MMRM)	
n	16
LS mean (SE)	79.95 (3.16)
95% CI of LS mean	(73.22, 86.68)
Absolute Change at Week 8 (MMRM)	
n	16
LS mean (SE)	2.34 (3.16)
95% CI of LS mean	(-4.39, 9.08)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	15
LS mean (SE)	81.38 (3.54)
95% CI of LS mean	(73.83, 88.94)
Absolute Change at Week 12 (MMRM)	
n	15
LS mean (SE)	3.78 (3.54)
95% CI of LS mean	(-3.78, 11.33)
Week 16 (MMRM)	
n	16
LS mean (SE)	84.11 (2.89)
95% CI of LS mean	(77.94, 90.29)
Absolute Change at Week 16 (MMRM)	
n	16
LS mean (SE)	6.51 (2.89)
95% CI of LS mean	(0.33, 12.69)
Week 24	
n	18
Mean (SD)	81.71 (13.03)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	16
Mean (SD)	6.25 (12.45)
Week 24 (MMRM)	
n	18
LS mean (SE)	83.85 (2.51)
95% CI of LS mean	(78.48, 89.23)
Absolute Change at Week 24 (MMRM)	
n	16
LS mean (SE)	6.25 (2.51)
95% CI of LS mean	(0.88, 11.62)
Absolute Change through Week 24 (MMRM)	
n	16
LS mean (SE)	6.38 (2.18)
95% CI of LS mean	(1.71, 11.05)
P-value	0.0109

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	89.10 (10.60)
Week 4 (MMRM)	
n	26
LS mean (SE)	87.61 (2.56)
95% CI of LS mean	(82.34, 92.88)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	-1.50 (2.56)
95% CI of LS mean	(-6.77, 3.78)
Week 8 (MMRM)	
n	26
LS mean (SE)	83.12 (3.39)
95% CI of LS mean	(76.13, 90.11)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	-5.98 (3.39)
95% CI of LS mean	(-12.97, 1.01)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	25
LS mean (SE)	85.23 (2.84)
95% CI of LS mean	(79.38, 91.09)
Absolute Change at Week 12 (MMRM)	
n	25
LS mean (SE)	-3.87 (2.84)
95% CI of LS mean	(-9.72, 1.99)
Week 16 (MMRM)	
n	26
LS mean (SE)	88.68 (3.23)
95% CI of LS mean	(82.01, 95.34)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	-0.43 (3.23)
95% CI of LS mean	(-7.09, 6.24)
Week 24	
n	27
Mean (SD)	90.33 (17.68)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	1.07 (18.26)
Week 24 (MMRM)	
n	27
LS mean (SE)	90.17 (3.43)
95% CI of LS mean	(83.10, 97.24)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	1.07 (3.43)
95% CI of LS mean	(-6.00, 8.14)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	0.32 (2.60)
95% CI of LS mean	(-5.04, 5.68)
P-value	0.9029

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	83.55 (14.53)
Week 4 (MMRM)	
n	26
LS mean (SE)	85.47 (2.75)
95% CI of LS mean	(79.78, 91.16)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	1.92 (2.75)
95% CI of LS mean	(-3.76, 7.61)
Week 8 (MMRM)	
n	26
LS mean (SE)	84.49 (3.15)
95% CI of LS mean	(77.98, 90.99)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	0.94 (3.15)
95% CI of LS mean	(-5.56, 7.44)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	85.90 (3.11)
95% CI of LS mean	(79.48, 92.31)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	2.35 (3.11)
95% CI of LS mean	(-4.07, 8.77)
Week 16 (MMRM)	
n	26
LS mean (SE)	89.32 (2.57)
95% CI of LS mean	(84.02, 94.61)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	5.77 (2.57)
95% CI of LS mean	(0.47, 11.06)
Week 24	
n	27
Mean (SD)	88.89 (13.25)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	6.41 (13.21)
Week 24 (MMRM)	
n	27
LS mean (SE)	89.96 (2.08)
95% CI of LS mean	(85.67, 94.25)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	6.41 (2.08)
95% CI of LS mean	(2.12, 10.70)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	6.09 (2.16)
95% CI of LS mean	(1.63, 10.55)
P-value	0.0094

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	85.34 (12.11)
Week 4 (MMRM)	
n	36
LS mean (SE)	83.95 (2.34)
95% CI of LS mean	(79.19, 88.71)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	-1.39 (2.34)
95% CI of LS mean	(-6.15, 3.37)
Week 8 (MMRM)	
n	36
LS mean (SE)	82.93 (2.69)
95% CI of LS mean	(77.47, 88.40)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	-2.41 (2.69)
95% CI of LS mean	(-7.87, 3.06)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	85.34 (2.73)
95% CI of LS mean	(79.80, 90.88)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	0.00 (2.73)
95% CI of LS mean	(-5.54, 5.54)
Week 16 (MMRM)	
n	36
LS mean (SE)	89.81 (2.46)
95% CI of LS mean	(84.81, 94.82)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	4.48 (2.46)
95% CI of LS mean	(-0.53, 9.49)
Week 24	
n	36
Mean (SD)	88.12 (17.22)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	2.78 (17.99)
Week 24 (MMRM)	
n	36
LS mean (SE)	88.12 (2.80)
95% CI of LS mean	(82.42, 93.82)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	2.78 (2.80)
95% CI of LS mean	(-2.92, 8.48)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	3.63 (2.22)
95% CI of LS mean	(-0.89, 8.15)
P-value	0.1122

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	16
Mean (SD)	88.54 (14.69)
Week 4 (MMRM)	
n	16
LS mean (SE)	92.36 (2.04)
95% CI of LS mean	(87.99, 96.73)
Absolute Change at Week 4 (MMRM)	
n	16
LS mean (SE)	3.82 (2.04)
95% CI of LS mean	(-0.55, 8.19)
Week 8 (MMRM)	
n	16
LS mean (SE)	85.76 (4.42)
95% CI of LS mean	(76.33, 95.20)
Absolute Change at Week 8 (MMRM)	
n	16
LS mean (SE)	-2.78 (4.42)
95% CI of LS mean	(-12.21, 6.66)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	15
LS mean (SE)	87.01 (3.25)
95% CI of LS mean	(79.98, 94.04)
Absolute Change at Week 12 (MMRM)	
n	15
LS mean (SE)	-1.53 (3.25)
95% CI of LS mean	(-8.57, 5.50)
Week 16 (MMRM)	
n	16
LS mean (SE)	87.15 (3.81)
95% CI of LS mean	(79.02, 95.28)
Absolute Change at Week 16 (MMRM)	
n	16
LS mean (SE)	-1.39 (3.81)
95% CI of LS mean	(-9.52, 6.74)
Week 24	
n	18
Mean (SD)	92.59 (11.11)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	16
Mean (SD)	5.90 (10.44)
Week 24 (MMRM)	
n	18
LS mean (SE)	94.44 (1.50)
95% CI of LS mean	(91.23, 97.66)
Absolute Change at Week 24 (MMRM)	
n	16
LS mean (SE)	5.90 (1.50)
95% CI of LS mean	(2.69, 9.12)
Absolute Change through Week 24 (MMRM)	
n	16
LS mean (SE)	2.26 (2.46)
95% CI of LS mean	(-2.98, 7.50)
P-value	0.3729

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	65.93 (17.85)
Week 4 (MMRM)	
n	26
LS mean (SE)	68.68 (2.67)
95% CI of LS mean	(63.17, 74.19)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	2.75 (2.67)
95% CI of LS mean	(-2.76, 8.25)
Week 8 (MMRM)	
n	26
LS mean (SE)	66.85 (2.59)
95% CI of LS mean	(61.51, 72.19)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	0.92 (2.59)
95% CI of LS mean	(-4.42, 6.26)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	25
LS mean (SE)	73.23 (2.81)
95% CI of LS mean	(67.43, 79.03)
Absolute Change at Week 12 (MMRM)	
n	25
LS mean (SE)	7.30 (2.81)
95% CI of LS mean	(1.50, 13.09)
Week 16 (MMRM)	
n	26
LS mean (SE)	76.19 (2.87)
95% CI of LS mean	(70.28, 82.10)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	10.26 (2.87)
95% CI of LS mean	(4.34, 16.17)
Week 24	
n	27
Mean (SD)	77.07 (15.40)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	11.90 (17.93)
Week 24 (MMRM)	
n	27
LS mean (SE)	77.84 (2.76)
95% CI of LS mean	(72.14, 83.54)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	11.90 (2.76)
95% CI of LS mean	(6.20, 17.61)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	11.08 (2.65)
95% CI of LS mean	(5.61, 16.55)
P-value	0.0003

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	64.47 (23.22)
Week 4 (MMRM)	
n	26
LS mean (SE)	65.20 (3.01)
95% CI of LS mean	(58.98, 71.43)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	0.73 (3.01)
95% CI of LS mean	(-5.49, 6.96)
Week 8 (MMRM)	
n	26
LS mean (SE)	69.96 (3.63)
95% CI of LS mean	(62.49, 77.44)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	5.49 (3.63)
95% CI of LS mean	(-1.98, 12.97)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	71.98 (3.18)
95% CI of LS mean	(65.42, 78.54)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	7.51 (3.18)
95% CI of LS mean	(0.95, 14.07)
Week 16 (MMRM)	
n	26
LS mean (SE)	68.86 (4.15)
95% CI of LS mean	(60.31, 77.42)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	4.40 (4.15)
95% CI of LS mean	(-4.16, 12.95)
Week 24	
n	27
Mean (SD)	71.78 (15.40)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	8.61 (23.21)
Week 24 (MMRM)	
n	27
LS mean (SE)	73.08 (2.82)
95% CI of LS mean	(67.22, 78.93)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	8.61 (2.82)
95% CI of LS mean	(2.75, 14.46)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	6.50 (3.12)
95% CI of LS mean	(0.05, 12.95)
P-value	0.0484

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	64.02 (21.25)
Week 4 (MMRM)	
n	36
LS mean (SE)	67.20 (2.32)
95% CI of LS mean	(62.48, 71.92)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	3.17 (2.32)
95% CI of LS mean	(-1.55, 7.89)
Week 8 (MMRM)	
n	36
LS mean (SE)	67.86 (3.02)
95% CI of LS mean	(61.73, 73.99)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	3.84 (3.02)
95% CI of LS mean	(-2.30, 9.97)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	72.49 (2.71)
95% CI of LS mean	(66.99, 77.98)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	8.47 (2.71)
95% CI of LS mean	(2.97, 13.96)
Week 16 (MMRM)	
n	36
LS mean (SE)	73.15 (3.27)
95% CI of LS mean	(66.50, 79.79)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	9.13 (3.27)
95% CI of LS mean	(2.48, 15.77)
Week 24	
n	36
Mean (SD)	75.40 (14.33)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	11.38 (21.43)
Week 24 (MMRM)	
n	36
LS mean (SE)	75.40 (2.40)
95% CI of LS mean	(70.50, 80.30)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	11.38 (2.40)
95% CI of LS mean	(6.47, 16.28)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	10.25 (2.61)
95% CI of LS mean	(4.93, 15.57)
P-value	0.0004

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	16
Mean (SD)	67.86 (19.17)
Week 4 (MMRM)	
n	16
LS mean (SE)	66.37 (3.92)
95% CI of LS mean	(57.94, 74.79)
Absolute Change at Week 4 (MMRM)	
n	16
LS mean (SE)	-1.49 (3.92)
95% CI of LS mean	(-9.91, 6.94)
Week 8 (MMRM)	
n	16
LS mean (SE)	69.64 (2.74)
95% CI of LS mean	(63.79, 75.49)
Absolute Change at Week 8 (MMRM)	
n	16
LS mean (SE)	1.79 (2.74)
95% CI of LS mean	(-4.06, 7.64)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	15
LS mean (SE)	72.98 (3.28)
95% CI of LS mean	(65.89, 80.07)
Absolute Change at Week 12 (MMRM)	
n	15
LS mean (SE)	5.12 (3.28)
95% CI of LS mean	(-1.97, 12.21)
Week 16 (MMRM)	
n	16
LS mean (SE)	71.13 (3.91)
95% CI of LS mean	(62.78, 79.48)
Absolute Change at Week 16 (MMRM)	
n	16
LS mean (SE)	3.27 (3.91)
95% CI of LS mean	(-5.07, 11.62)
Week 24	
n	18
Mean (SD)	72.49 (17.86)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	16
Mean (SD)	7.74 (19.04)
Week 24 (MMRM)	
n	18
LS mean (SE)	75.60 (3.67)
95% CI of LS mean	(67.76, 83.43)
Absolute Change at Week 24 (MMRM)	
n	16
LS mean (SE)	7.74 (3.67)
95% CI of LS mean	(-0.10, 15.57)
Absolute Change through Week 24 (MMRM)	
n	16
LS mean (SE)	5.51 (3.41)
95% CI of LS mean	(-1.77, 12.78)
P-value	0.1274

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	77.35 (22.55)
Week 4 (MMRM)	
n	26
LS mean (SE)	77.78 (2.62)
95% CI of LS mean	(72.38, 83.18)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	0.43 (2.62)
95% CI of LS mean	(-4.97, 5.83)
Week 8 (MMRM)	
n	26
LS mean (SE)	78.63 (3.44)
95% CI of LS mean	(71.53, 85.73)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	1.28 (3.44)
95% CI of LS mean	(-5.82, 8.38)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	25
LS mean (SE)	80.49 (4.39)
95% CI of LS mean	(71.45, 89.52)
Absolute Change at Week 12 (MMRM)	
n	25
LS mean (SE)	3.14 (4.39)
95% CI of LS mean	(-5.90, 12.17)
Week 16 (MMRM)	
n	26
LS mean (SE)	80.77 (4.41)
95% CI of LS mean	(71.69, 89.84)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	3.42 (4.41)
95% CI of LS mean	(-5.66, 12.49)
Week 24	
n	27
Mean (SD)	82.72 (22.92)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	5.56 (25.39)
Week 24 (MMRM)	
n	27
LS mean (SE)	82.91 (4.39)
95% CI of LS mean	(73.85, 91.96)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	5.56 (4.39)
95% CI of LS mean	(-3.50, 14.61)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	4.49 (4.02)
95% CI of LS mean	(-3.81, 12.79)
P-value	0.2757

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	73.08 (21.58)
Week 4 (MMRM)	
n	26
LS mean (SE)	78.63 (3.98)
95% CI of LS mean	(70.40, 86.87)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	5.56 (3.98)
95% CI of LS mean	(-2.68, 13.79)
Week 8 (MMRM)	
n	26
LS mean (SE)	76.71 (3.47)
95% CI of LS mean	(69.56, 83.86)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	3.63 (3.47)
95% CI of LS mean	(-3.52, 10.79)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	78.21 (2.59)
95% CI of LS mean	(72.85, 83.56)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	5.13 (2.59)
95% CI of LS mean	(-0.23, 10.48)
Week 16 (MMRM)	
n	26
LS mean (SE)	78.63 (3.67)
95% CI of LS mean	(71.07, 86.19)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	5.56 (3.67)
95% CI of LS mean	(-2.00, 13.12)
Week 24	
n	27
Mean (SD)	78.60 (21.11)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	5.13 (17.84)
Week 24 (MMRM)	
n	27
LS mean (SE)	78.21 (3.24)
95% CI of LS mean	(71.53, 84.88)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	5.13 (3.24)
95% CI of LS mean	(-1.55, 11.81)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	5.34 (2.88)
95% CI of LS mean	(-0.61, 11.29)
P-value	0.0763

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	74.38 (22.51)
Week 4 (MMRM)	
n	36
LS mean (SE)	73.46 (2.74)
95% CI of LS mean	(67.88, 79.03)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	-0.93 (2.74)
95% CI of LS mean	(-6.50, 4.65)
Week 8 (MMRM)	
n	36
LS mean (SE)	73.61 (2.91)
95% CI of LS mean	(67.69, 79.53)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	-0.77 (2.91)
95% CI of LS mean	(-6.69, 5.15)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	76.23 (3.04)
95% CI of LS mean	(70.05, 82.42)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	1.85 (3.04)
95% CI of LS mean	(-4.33, 8.04)
Week 16 (MMRM)	
n	36
LS mean (SE)	79.63 (3.47)
95% CI of LS mean	(72.59, 86.67)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	5.25 (3.47)
95% CI of LS mean	(-1.79, 12.28)
Week 24	
n	36
Mean (SD)	77.47 (24.70)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	3.09 (20.85)
Week 24 (MMRM)	
n	36
LS mean (SE)	77.47 (3.27)
95% CI of LS mean	(70.82, 84.11)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	3.09 (3.27)
95% CI of LS mean	(-3.56, 9.73)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	4.17 (2.98)
95% CI of LS mean	(-1.88, 10.22)
P-value	0.1707

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	16
Mean (SD)	77.08 (21.26)
Week 4 (MMRM)	
n	16
LS mean (SE)	88.89 (2.59)
95% CI of LS mean	(83.34, 94.44)
Absolute Change at Week 4 (MMRM)	
n	16
LS mean (SE)	11.81 (2.59)
95% CI of LS mean	(6.26, 17.35)
Week 8 (MMRM)	
n	16
LS mean (SE)	86.81 (3.92)
95% CI of LS mean	(78.35, 95.27)
Absolute Change at Week 8 (MMRM)	
n	16
LS mean (SE)	9.72 (3.92)
95% CI of LS mean	(1.26, 18.18)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	15
LS mean (SE)	86.13 (4.14)
95% CI of LS mean	(77.29, 94.97)
Absolute Change at Week 12 (MMRM)	
n	15
LS mean (SE)	9.05 (4.14)
95% CI of LS mean	(0.21, 17.89)
Week 16 (MMRM)	
n	16
LS mean (SE)	79.86 (4.93)
95% CI of LS mean	(69.33, 90.39)
Absolute Change at Week 16 (MMRM)	
n	16
LS mean (SE)	2.78 (4.93)
95% CI of LS mean	(-7.75, 13.31)
Week 24	
n	18
Mean (SD)	87.04 (13.34)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	16
Mean (SD)	10.42 (23.47)
Week 24 (MMRM)	
n	18
LS mean (SE)	87.50 (3.59)
95% CI of LS mean	(79.80, 95.20)
Absolute Change at Week 24 (MMRM)	
n	16
LS mean (SE)	10.42 (3.59)
95% CI of LS mean	(2.72, 18.11)
Absolute Change through Week 24 (MMRM)	
n	16
LS mean (SE)	6.60 (3.78)
95% CI of LS mean	(-1.47, 14.66)
P-value	0.1017

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Body (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0462
Region (North America vs. Rest of the World)	0.1403
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Body (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.9881
Region (North America vs. Rest of the World)	0.2890
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Digestion (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

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Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0852
Region (North America vs. Rest of the World)	0.7233
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Eat (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.4944
Region (North America vs. Rest of the World)	0.8943
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Emotion (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.6048
Region (North America vs. Rest of the World)	0.1919
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Health Perceptions (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.3077
Region (North America vs. Rest of the World)	0.5926
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Physical (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

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Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: School (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.9604
Region (North America vs. Rest of the World)	0.4461
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R School (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.4092
Region (North America vs. Rest of the World)	0.8400
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Treatment Burden (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

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Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.5284
Region (North America vs. Rest of the World)	0.4631
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Vitality (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

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Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.5107
Region (North America vs. Rest of the World)	0.1630
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Weight (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	79.42 (27.16)
Week 4 (MMRM)	
n	27
LS mean (SE)	86.01 (2.37)
95% CI of LS mean	(81.13, 90.89)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	6.58 (2.37)
95% CI of LS mean	(1.70, 11.47)
Week 8 (MMRM)	
n	27
LS mean (SE)	80.66 (3.08)
95% CI of LS mean	(74.32, 87.00)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	1.23 (3.08)
95% CI of LS mean	(-5.11, 7.57)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	85.89 (2.29)
95% CI of LS mean	(81.17, 90.60)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	6.46 (2.29)
95% CI of LS mean	(1.75, 11.18)
Week 16 (MMRM)	
n	27
LS mean (SE)	90.12 (3.38)
95% CI of LS mean	(83.12, 97.13)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	10.70 (3.38)
95% CI of LS mean	(3.69, 17.71)
Week 24	
n	27
Mean (SD)	88.07 (18.98)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	8.64 (18.58)
Week 24 (MMRM)	
n	27
LS mean (SE)	88.07 (2.53)
95% CI of LS mean	(82.86, 93.27)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	8.64 (2.53)
95% CI of LS mean	(3.44, 13.85)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	9.67 (2.61)
95% CI of LS mean	(4.27, 15.07)
P-value	0.0012

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	78.81 (26.33)
Week 4 (MMRM)	
n	27
LS mean (SE)	77.37 (2.79)
95% CI of LS mean	(71.58, 83.15)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-1.44 (2.79)
95% CI of LS mean	(-7.22, 4.34)
Week 8 (MMRM)	
n	27
LS mean (SE)	81.89 (3.49)
95% CI of LS mean	(74.66, 89.12)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	3.09 (3.49)
95% CI of LS mean	(-4.14, 10.32)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	82.30 (3.36)
95% CI of LS mean	(75.38, 89.23)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	3.50 (3.36)
95% CI of LS mean	(-3.43, 10.42)
Week 16 (MMRM)	
n	27
LS mean (SE)	81.48 (2.93)
95% CI of LS mean	(75.46, 87.50)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	2.67 (2.93)
95% CI of LS mean	(-3.34, 8.69)
Week 24	
n	27
Mean (SD)	76.95 (19.47)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	-1.85 (21.85)
Week 24 (MMRM)	
n	27
LS mean (SE)	76.95 (3.17)
95% CI of LS mean	(70.41, 83.50)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	-1.85 (3.17)
95% CI of LS mean	(-8.40, 4.70)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	0.41 (2.56)
95% CI of LS mean	(-4.87, 5.70)
P-value	0.8738

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	77.47 (26.36)
Week 4 (MMRM)	
n	36
LS mean (SE)	80.56 (2.40)
95% CI of LS mean	(75.68, 85.44)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	3.09 (2.40)
95% CI of LS mean	(-1.79, 7.97)
Week 8 (MMRM)	
n	36
LS mean (SE)	78.40 (2.34)
95% CI of LS mean	(73.64, 83.15)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	0.93 (2.34)
95% CI of LS mean	(-3.83, 5.68)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	80.86 (2.75)
95% CI of LS mean	(75.27, 86.45)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	3.40 (2.75)
95% CI of LS mean	(-2.20, 8.99)
Week 16 (MMRM)	
n	36
LS mean (SE)	85.80 (3.08)
95% CI of LS mean	(79.54, 92.07)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	8.33 (3.08)
95% CI of LS mean	(2.07, 14.60)
Week 24	
n	36
Mean (SD)	79.63 (21.33)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	2.16 (20.88)
Week 24 (MMRM)	
n	36
LS mean (SE)	79.63 (2.78)
95% CI of LS mean	(73.99, 85.27)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	2.16 (2.78)
95% CI of LS mean	(-3.48, 7.80)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	5.25 (2.65)
95% CI of LS mean	(-0.14, 10.63)
P-value	0.0557

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	82.41 (27.23)
Week 4 (MMRM)	
n	18
LS mean (SE)	83.95 (3.11)
95% CI of LS mean	(77.32, 90.58)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	1.54 (3.11)
95% CI of LS mean	(-5.09, 8.17)
Week 8 (MMRM)	
n	18
LS mean (SE)	87.04 (5.13)
95% CI of LS mean	(76.14, 97.94)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	4.63 (5.13)
95% CI of LS mean	(-6.27, 15.53)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	90.69 (2.19)
95% CI of LS mean	(85.94, 95.45)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	8.29 (2.19)
95% CI of LS mean	(3.53, 13.04)
Week 16 (MMRM)	
n	18
LS mean (SE)	85.80 (3.17)
95% CI of LS mean	(79.11, 92.50)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	3.40 (3.17)
95% CI of LS mean	(-3.30, 10.09)
Week 24	
n	18
Mean (SD)	88.27 (15.47)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	5.86 (20.92)
Week 24 (MMRM)	
n	18
LS mean (SE)	88.27 (3.16)
95% CI of LS mean	(81.56, 94.98)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	5.86 (3.16)
95% CI of LS mean	(-0.85, 12.58)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	4.63 (2.46)
95% CI of LS mean	(-0.62, 9.88)
P-value	0.0798

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	80.66 (16.76)
Week 4 (MMRM)	
n	27
LS mean (SE)	78.19 (4.11)
95% CI of LS mean	(69.74, 86.64)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-2.47 (4.11)
95% CI of LS mean	(-10.92, 5.98)
Week 8 (MMRM)	
n	27
LS mean (SE)	81.89 (2.84)
95% CI of LS mean	(76.05, 87.74)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	1.23 (2.84)
95% CI of LS mean	(-4.61, 7.08)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	83.37 (3.03)
95% CI of LS mean	(77.13, 89.61)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	2.72 (3.03)
95% CI of LS mean	(-3.53, 8.96)
Week 16 (MMRM)	
n	27
LS mean (SE)	86.01 (2.27)
95% CI of LS mean	(81.35, 90.67)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	5.35 (2.27)
95% CI of LS mean	(0.69, 10.01)
Week 24	
n	27
Mean (SD)	81.89 (14.17)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	1.23 (16.11)
Week 24 (MMRM)	
n	27
LS mean (SE)	81.89 (2.44)
95% CI of LS mean	(76.87, 86.91)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	1.23 (2.44)
95% CI of LS mean	(-3.79, 6.25)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	3.29 (2.07)
95% CI of LS mean	(-0.98, 7.56)
P-value	0.1248

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	84.36 (18.30)
Week 4 (MMRM)	
n	27
LS mean (SE)	88.07 (1.89)
95% CI of LS mean	(84.17, 91.97)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	3.70 (1.89)
95% CI of LS mean	(-0.20, 7.60)
Week 8 (MMRM)	
n	27
LS mean (SE)	83.13 (2.52)
95% CI of LS mean	(77.95, 88.30)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	-1.23 (2.52)
95% CI of LS mean	(-6.41, 3.94)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	86.01 (2.31)
95% CI of LS mean	(81.26, 90.76)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	1.65 (2.31)
95% CI of LS mean	(-3.10, 6.40)
Week 16 (MMRM)	
n	27
LS mean (SE)	85.19 (2.32)
95% CI of LS mean	(80.41, 89.96)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	0.82 (2.32)
95% CI of LS mean	(-3.95, 5.60)
Week 24	
n	27
Mean (SD)	81.07 (15.66)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	-3.29 (17.92)
Week 24 (MMRM)	
n	27
LS mean (SE)	81.07 (2.71)
95% CI of LS mean	(75.51, 86.63)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	-3.29 (2.71)
95% CI of LS mean	(-8.86, 2.27)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	-1.23 (2.12)
95% CI of LS mean	(-5.60, 3.13)
P-value	0.5655

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	82.10 (18.65)
Week 4 (MMRM)	
n	36
LS mean (SE)	85.80 (1.98)
95% CI of LS mean	(81.77, 89.83)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	3.70 (1.98)
95% CI of LS mean	(-0.33, 7.73)
Week 8 (MMRM)	
n	36
LS mean (SE)	82.41 (2.28)
95% CI of LS mean	(77.77, 87.04)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	0.31 (2.28)
95% CI of LS mean	(-4.32, 4.94)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	83.64 (2.28)
95% CI of LS mean	(79.00, 88.29)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	1.54 (2.28)
95% CI of LS mean	(-3.10, 6.19)
Week 16 (MMRM)	
n	36
LS mean (SE)	86.42 (1.89)
95% CI of LS mean	(82.57, 90.27)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	4.32 (1.89)
95% CI of LS mean	(0.47, 8.17)
Week 24	
n	36
Mean (SD)	81.48 (14.30)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	-0.62 (17.41)
Week 24 (MMRM)	
n	36
LS mean (SE)	81.48 (2.13)
95% CI of LS mean	(77.16, 85.80)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	-0.62 (2.13)
95% CI of LS mean	(-4.94, 3.71)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	1.85 (1.75)
95% CI of LS mean	(-1.70, 5.40)
P-value	0.2968

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	83.33 (15.36)
Week 4 (MMRM)	
n	18
LS mean (SE)	77.78 (5.60)
95% CI of LS mean	(65.96, 89.60)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	-5.56 (5.60)
95% CI of LS mean	(-17.38, 6.27)
Week 8 (MMRM)	
n	18
LS mean (SE)	82.72 (3.30)
95% CI of LS mean	(75.68, 89.75)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	-0.62 (3.30)
95% CI of LS mean	(-7.65, 6.42)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	87.15 (3.35)
95% CI of LS mean	(80.01, 94.29)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	3.82 (3.35)
95% CI of LS mean	(-3.32, 10.96)
Week 16 (MMRM)	
n	18
LS mean (SE)	83.95 (3.03)
95% CI of LS mean	(77.54, 90.36)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	0.62 (3.03)
95% CI of LS mean	(-5.80, 7.03)
Week 24	
n	18
Mean (SD)	81.48 (16.17)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	-1.85 (16.72)
Week 24 (MMRM)	
n	18
LS mean (SE)	81.48 (3.55)
95% CI of LS mean	(73.96, 89.00)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	-1.85 (3.55)
95% CI of LS mean	(-9.37, 5.67)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-0.62 (2.82)
95% CI of LS mean	(-6.60, 5.37)
P-value	0.8295

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	76.54 (24.57)
Week 4 (MMRM)	
n	27
LS mean (SE)	79.01 (3.24)
95% CI of LS mean	(72.34, 85.69)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	2.47 (3.24)
95% CI of LS mean	(-4.20, 9.14)
Week 8 (MMRM)	
n	27
LS mean (SE)	76.54 (4.17)
95% CI of LS mean	(67.95, 85.14)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	0.00 (4.17)
95% CI of LS mean	(-8.59, 8.59)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	79.71 (3.59)
95% CI of LS mean	(72.29, 87.14)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	3.17 (3.59)
95% CI of LS mean	(-4.25, 10.60)
Week 16 (MMRM)	
n	27
LS mean (SE)	80.25 (2.77)
95% CI of LS mean	(74.56, 85.94)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	3.70 (2.77)
95% CI of LS mean	(-1.99, 9.39)
Week 24	
n	27
Mean (SD)	82.10 (20.11)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	5.56 (19.61)
Week 24 (MMRM)	
n	27
LS mean (SE)	82.10 (3.04)
95% CI of LS mean	(75.84, 88.36)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	5.56 (3.04)
95% CI of LS mean	(-0.71, 11.82)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	4.63 (2.41)
95% CI of LS mean	(-0.34, 9.60)
P-value	0.0664

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	76.54 (27.83)
Week 4 (MMRM)	
n	27
LS mean (SE)	72.22 (3.21)
95% CI of LS mean	(65.63, 78.81)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-4.32 (3.21)
95% CI of LS mean	(-10.91, 2.27)
Week 8 (MMRM)	
n	27
LS mean (SE)	74.07 (3.43)
95% CI of LS mean	(67.03, 81.12)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	-2.47 (3.43)
95% CI of LS mean	(-9.51, 4.57)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	71.60 (3.33)
95% CI of LS mean	(64.75, 78.46)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	-4.94 (3.33)
95% CI of LS mean	(-11.79, 1.92)
Week 16 (MMRM)	
n	27
LS mean (SE)	77.16 (2.43)
95% CI of LS mean	(72.16, 82.16)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	0.62 (2.43)
95% CI of LS mean	(-4.38, 5.62)
Week 24	
n	27
Mean (SD)	78.40 (25.24)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	1.85 (19.79)
Week 24 (MMRM)	
n	27
LS mean (SE)	78.40 (3.37)
95% CI of LS mean	(71.46, 85.33)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	1.85 (3.37)
95% CI of LS mean	(-5.08, 8.78)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	1.23 (2.54)
95% CI of LS mean	(-4.00, 6.46)
P-value	0.6314

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	74.54 (26.27)
Week 4 (MMRM)	
n	36
LS mean (SE)	74.54 (2.84)
95% CI of LS mean	(68.77, 80.31)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	0.00 (2.84)
95% CI of LS mean	(-5.77, 5.77)
Week 8 (MMRM)	
n	36
LS mean (SE)	75.46 (3.00)
95% CI of LS mean	(69.37, 81.55)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	0.93 (3.00)
95% CI of LS mean	(-5.16, 7.01)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	74.07 (2.55)
95% CI of LS mean	(68.88, 79.27)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	-0.46 (2.55)
95% CI of LS mean	(-5.66, 4.73)
Week 16 (MMRM)	
n	36
LS mean (SE)	78.24 (2.11)
95% CI of LS mean	(73.95, 82.53)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	3.70 (2.11)
95% CI of LS mean	(-0.59, 8.00)
Week 24	
n	36
Mean (SD)	81.48 (21.00)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	6.94 (17.98)
Week 24 (MMRM)	
n	36
LS mean (SE)	81.48 (2.42)
95% CI of LS mean	(76.57, 86.40)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	6.94 (2.42)
95% CI of LS mean	(2.03, 11.86)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	5.32 (1.94)
95% CI of LS mean	(1.39, 9.26)
P-value	0.0095

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	80.56 (25.72)
Week 4 (MMRM)	
n	18
LS mean (SE)	77.78 (3.87)
95% CI of LS mean	(69.61, 85.94)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	-2.78 (3.87)
95% CI of LS mean	(-10.94, 5.39)
Week 8 (MMRM)	
n	18
LS mean (SE)	75.00 (5.41)
95% CI of LS mean	(63.56, 86.44)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	-5.56 (5.41)
95% CI of LS mean	(-16.99, 5.88)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	79.29 (5.55)
95% CI of LS mean	(67.55, 91.02)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	-1.27 (5.55)
95% CI of LS mean	(-13.01, 10.47)
Week 16 (MMRM)	
n	18
LS mean (SE)	79.63 (3.77)
95% CI of LS mean	(71.64, 87.62)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	-0.93 (3.77)
95% CI of LS mean	(-8.92, 7.06)
Week 24	
n	18
Mean (SD)	77.78 (26.20)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	-2.78 (21.58)
Week 24 (MMRM)	
n	18
LS mean (SE)	77.78 (4.70)
95% CI of LS mean	(67.86, 87.69)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	-2.78 (4.70)
95% CI of LS mean	(-12.69, 7.14)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-1.85 (3.64)
95% CI of LS mean	(-9.54, 5.83)
P-value	0.6172

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	85.68 (13.80)
Week 4 (MMRM)	
n	27
LS mean (SE)	86.91 (1.58)
95% CI of LS mean	(83.64, 90.19)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	1.23 (1.58)
95% CI of LS mean	(-2.04, 4.51)
Week 8 (MMRM)	
n	27
LS mean (SE)	85.93 (2.01)
95% CI of LS mean	(81.79, 90.06)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	0.25 (2.01)
95% CI of LS mean	(-3.89, 4.38)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	89.06 (1.88)
95% CI of LS mean	(85.19, 92.94)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	3.39 (1.88)
95% CI of LS mean	(-0.49, 7.26)
Week 16 (MMRM)	
n	27
LS mean (SE)	88.64 (2.26)
95% CI of LS mean	(84.00, 93.28)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	2.96 (2.26)
95% CI of LS mean	(-1.68, 7.60)
Week 24	
n	27
Mean (SD)	89.88 (9.31)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	4.20 (13.22)
Week 24 (MMRM)	
n	27
LS mean (SE)	89.88 (1.74)
95% CI of LS mean	(86.27, 93.48)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	4.20 (1.74)
95% CI of LS mean	(0.60, 7.80)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	3.58 (1.45)
95% CI of LS mean	(0.60, 6.56)
P-value	0.0206

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	84.51 (14.63)
Week 4 (MMRM)	
n	27
LS mean (SE)	84.69 (1.89)
95% CI of LS mean	(80.80, 88.59)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	0.19 (1.89)
95% CI of LS mean	(-3.71, 4.08)
Week 8 (MMRM)	
n	27
LS mean (SE)	84.57 (1.32)
95% CI of LS mean	(81.86, 87.28)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	0.06 (1.32)
95% CI of LS mean	(-2.65, 2.77)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	87.65 (1.91)
95% CI of LS mean	(83.73, 91.58)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	3.15 (1.91)
95% CI of LS mean	(-0.77, 7.07)
Week 16 (MMRM)	
n	27
LS mean (SE)	88.64 (1.41)
95% CI of LS mean	(85.74, 91.54)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	4.14 (1.41)
95% CI of LS mean	(1.24, 7.03)
Week 24	
n	27
Mean (SD)	87.41 (11.30)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	2.90 (11.58)
Week 24 (MMRM)	
n	27
LS mean (SE)	87.41 (1.73)
95% CI of LS mean	(83.84, 90.97)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	2.90 (1.73)
95% CI of LS mean	(-0.66, 6.47)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	3.52 (1.11)
95% CI of LS mean	(1.24, 5.80)
P-value	0.0040

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	85.60 (14.61)
Week 4 (MMRM)	
n	36
LS mean (SE)	86.11 (1.40)
95% CI of LS mean	(83.26, 88.97)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	0.51 (1.40)
95% CI of LS mean	(-2.35, 3.36)
Week 8 (MMRM)	
n	36
LS mean (SE)	85.28 (1.40)
95% CI of LS mean	(82.43, 88.12)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	-0.32 (1.40)
95% CI of LS mean	(-3.17, 2.52)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	88.15 (1.47)
95% CI of LS mean	(85.15, 91.14)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	2.55 (1.47)
95% CI of LS mean	(-0.45, 5.54)
Week 16 (MMRM)	
n	36
LS mean (SE)	90.19 (1.33)
95% CI of LS mean	(87.48, 92.90)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	4.58 (1.33)
95% CI of LS mean	(1.87, 7.29)
Week 24	
n	36
Mean (SD)	88.70 (9.93)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	3.10 (10.62)
Week 24 (MMRM)	
n	36
LS mean (SE)	88.70 (1.21)
95% CI of LS mean	(86.24, 91.17)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	3.10 (1.21)
95% CI of LS mean	(0.64, 5.57)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	3.84 (1.07)
95% CI of LS mean	(1.66, 6.02)
P-value	0.0011

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	84.07 (13.36)
Week 4 (MMRM)	
n	18
LS mean (SE)	85.19 (2.42)
95% CI of LS mean	(80.07, 90.30)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	1.11 (2.42)
95% CI of LS mean	(-4.00, 6.22)
Week 8 (MMRM)	
n	18
LS mean (SE)	85.19 (2.36)
95% CI of LS mean	(80.16, 90.21)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	1.11 (2.36)
95% CI of LS mean	(-3.91, 6.13)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	88.69 (2.80)
95% CI of LS mean	(82.77, 94.61)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	4.62 (2.80)
95% CI of LS mean	(-1.31, 10.54)
Week 16 (MMRM)	
n	18
LS mean (SE)	85.56 (2.81)
95% CI of LS mean	(79.58, 91.53)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	1.48 (2.81)
95% CI of LS mean	(-4.49, 7.46)
Week 24	
n	18
Mean (SD)	88.52 (11.39)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	4.44 (15.51)
Week 24 (MMRM)	
n	18
LS mean (SE)	88.52 (2.90)
95% CI of LS mean	(82.34, 94.70)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	4.44 (2.90)
95% CI of LS mean	(-1.73, 10.62)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	2.96 (1.68)
95% CI of LS mean	(-0.60, 6.53)
P-value	0.0971

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	86.01 (14.65)
Week 4 (MMRM)	
n	27
LS mean (SE)	83.13 (2.94)
95% CI of LS mean	(77.08, 89.17)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-2.88 (2.94)
95% CI of LS mean	(-8.92, 3.16)
Week 8 (MMRM)	
n	27
LS mean (SE)	85.60 (2.52)
95% CI of LS mean	(80.42, 90.77)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	-0.41 (2.52)
95% CI of LS mean	(-5.59, 4.76)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	87.89 (2.01)
95% CI of LS mean	(83.77, 92.02)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	1.88 (2.01)
95% CI of LS mean	(-2.24, 6.01)
Week 16 (MMRM)	
n	27
LS mean (SE)	90.12 (2.13)
95% CI of LS mean	(85.74, 94.51)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	4.12 (2.13)
95% CI of LS mean	(-0.27, 8.50)
Week 24	
n	27
Mean (SD)	90.12 (14.89)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	4.12 (14.83)
Week 24 (MMRM)	
n	27
LS mean (SE)	90.12 (2.51)
95% CI of LS mean	(84.96, 95.29)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	4.12 (2.51)
95% CI of LS mean	(-1.05, 9.28)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	4.12 (1.85)
95% CI of LS mean	(0.32, 7.92)
P-value	0.0349

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	87.24 (12.59)
Week 4 (MMRM)	
n	27
LS mean (SE)	83.54 (2.39)
95% CI of LS mean	(78.62, 88.46)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-3.70 (2.39)
95% CI of LS mean	(-8.62, 1.21)
Week 8 (MMRM)	
n	27
LS mean (SE)	89.30 (1.68)
95% CI of LS mean	(85.85, 92.75)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	2.06 (1.68)
95% CI of LS mean	(-1.39, 5.51)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	86.01 (2.84)
95% CI of LS mean	(80.17, 91.84)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	-1.23 (2.84)
95% CI of LS mean	(-7.07, 4.60)
Week 16 (MMRM)	
n	27
LS mean (SE)	88.48 (1.73)
95% CI of LS mean	(84.91, 92.04)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	1.23 (1.73)
95% CI of LS mean	(-2.33, 4.80)
Week 24	
n	27
Mean (SD)	83.95 (20.05)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	-3.29 (20.86)
Week 24 (MMRM)	
n	27
LS mean (SE)	83.95 (3.81)
95% CI of LS mean	(76.13, 91.78)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	-3.29 (3.81)
95% CI of LS mean	(-11.12, 4.53)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	-1.03 (2.34)
95% CI of LS mean	(-5.84, 3.78)
P-value	0.6636

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	86.73 (12.41)
Week 4 (MMRM)	
n	36
LS mean (SE)	83.33 (2.34)
95% CI of LS mean	(78.58, 88.09)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	-3.40 (2.34)
95% CI of LS mean	(-8.15, 1.36)
Week 8 (MMRM)	
n	36
LS mean (SE)	87.35 (1.87)
95% CI of LS mean	(83.54, 91.15)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	0.62 (1.87)
95% CI of LS mean	(-3.19, 4.42)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	87.65 (2.12)
95% CI of LS mean	(83.36, 91.95)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	0.93 (2.12)
95% CI of LS mean	(-3.37, 5.22)
Week 16 (MMRM)	
n	36
LS mean (SE)	91.36 (1.52)
95% CI of LS mean	(88.27, 94.45)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	4.63 (1.52)
95% CI of LS mean	(1.54, 7.72)
Week 24	
n	36
Mean (SD)	90.43 (15.29)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	3.70 (14.55)
Week 24 (MMRM)	
n	36
LS mean (SE)	90.43 (2.27)
95% CI of LS mean	(85.83, 95.04)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	3.70 (2.27)
95% CI of LS mean	(-0.90, 8.31)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	4.17 (1.56)
95% CI of LS mean	(1.00, 7.34)
P-value	0.0115

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	86.42 (15.97)
Week 4 (MMRM)	
n	18
LS mean (SE)	83.33 (3.24)
95% CI of LS mean	(76.48, 90.18)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	-3.09 (3.24)
95% CI of LS mean	(-9.93, 3.76)
Week 8 (MMRM)	
n	18
LS mean (SE)	87.65 (2.62)
95% CI of LS mean	(82.12, 93.19)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	1.23 (2.62)
95% CI of LS mean	(-4.30, 6.77)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	85.64 (3.19)
95% CI of LS mean	(78.90, 92.38)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	-0.78 (3.19)
95% CI of LS mean	(-7.52, 5.96)
Week 16 (MMRM)	
n	18
LS mean (SE)	85.19 (2.60)
95% CI of LS mean	(79.68, 90.69)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	-1.23 (2.60)
95% CI of LS mean	(-6.74, 4.27)
Week 24	
n	18
Mean (SD)	80.25 (20.72)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	-6.17 (23.25)
Week 24 (MMRM)	
n	18
LS mean (SE)	80.25 (4.91)
95% CI of LS mean	(69.89, 90.61)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	-6.17 (4.91)
95% CI of LS mean	(-16.53, 4.19)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-3.70 (2.92)
95% CI of LS mean	(-9.87, 2.46)
P-value	0.2219

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	91.51 (11.87)
Week 4 (MMRM)	
n	27
LS mean (SE)	92.75 (1.72)
95% CI of LS mean	(89.19, 96.30)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	1.23 (1.72)
95% CI of LS mean	(-2.32, 4.79)
Week 8 (MMRM)	
n	27
LS mean (SE)	89.81 (1.99)
95% CI of LS mean	(85.72, 93.91)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	-1.70 (1.99)
95% CI of LS mean	(-5.80, 2.40)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	92.22 (1.88)
95% CI of LS mean	(88.34, 96.10)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	0.71 (1.88)
95% CI of LS mean	(-3.17, 4.59)
Week 16 (MMRM)	
n	27
LS mean (SE)	93.98 (2.26)
95% CI of LS mean	(89.29, 98.68)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	2.47 (2.26)
95% CI of LS mean	(-2.22, 7.16)
Week 24	
n	27
Mean (SD)	92.28 (14.70)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	0.77 (9.81)
Week 24 (MMRM)	
n	27
LS mean (SE)	92.28 (1.95)
95% CI of LS mean	(88.27, 96.30)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	0.77 (1.95)
95% CI of LS mean	(-3.24, 4.79)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	1.62 (1.55)
95% CI of LS mean	(-1.58, 4.82)
P-value	0.3065

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	89.81 (17.84)
Week 4 (MMRM)	
n	27
LS mean (SE)	89.51 (2.67)
95% CI of LS mean	(84.01, 95.00)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-0.31 (2.67)
95% CI of LS mean	(-5.80, 5.18)
Week 8 (MMRM)	
n	27
LS mean (SE)	91.38 (2.10)
95% CI of LS mean	(87.05, 95.71)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	1.57 (2.10)
95% CI of LS mean	(-2.77, 5.90)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	95.68 (0.83)
95% CI of LS mean	(93.97, 97.39)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	5.86 (0.83)
95% CI of LS mean	(4.15, 7.58)
Week 16 (MMRM)	
n	27
LS mean (SE)	95.06 (1.67)
95% CI of LS mean	(91.63, 98.50)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	5.25 (1.67)
95% CI of LS mean	(1.81, 8.68)
Week 24	
n	27
Mean (SD)	90.90 (15.46)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	1.08 (14.04)
Week 24 (MMRM)	
n	27
LS mean (SE)	90.90 (2.48)
95% CI of LS mean	(85.78, 96.01)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	1.08 (2.48)
95% CI of LS mean	(-4.03, 6.19)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	3.16 (1.49)
95% CI of LS mean	(0.09, 6.24)
P-value	0.0443

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	90.63 (15.73)
Week 4 (MMRM)	
n	36
LS mean (SE)	90.74 (1.78)
95% CI of LS mean	(87.12, 94.36)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	0.12 (1.78)
95% CI of LS mean	(-3.50, 3.74)
Week 8 (MMRM)	
n	36
LS mean (SE)	90.18 (1.89)
95% CI of LS mean	(86.33, 94.03)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	-0.45 (1.89)
95% CI of LS mean	(-4.29, 3.40)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	94.21 (1.11)
95% CI of LS mean	(91.97, 96.46)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	3.59 (1.11)
95% CI of LS mean	(1.34, 5.83)
Week 16 (MMRM)	
n	36
LS mean (SE)	96.06 (0.96)
95% CI of LS mean	(94.10, 98.03)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	5.44 (0.96)
95% CI of LS mean	(3.47, 7.41)
Week 24	
n	36
Mean (SD)	92.13 (15.42)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	1.50 (9.35)
Week 24 (MMRM)	
n	36
LS mean (SE)	92.13 (1.67)
95% CI of LS mean	(88.72, 95.54)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	1.50 (1.67)
95% CI of LS mean	(-1.90, 4.91)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	3.47 (0.98)
95% CI of LS mean	(1.48, 5.46)
P-value	0.0012

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	90.74 (13.97)
Week 4 (MMRM)	
n	18
LS mean (SE)	91.90 (2.31)
95% CI of LS mean	(87.02, 96.77)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	1.16 (2.31)
95% CI of LS mean	(-3.72, 6.03)
Week 8 (MMRM)	
n	18
LS mean (SE)	91.44 (1.22)
95% CI of LS mean	(88.86, 94.01)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	0.69 (1.22)
95% CI of LS mean	(-1.88, 3.27)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	93.68 (2.20)
95% CI of LS mean	(89.03, 98.34)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	2.94 (2.20)
95% CI of LS mean	(-1.71, 7.59)
Week 16 (MMRM)	
n	18
LS mean (SE)	91.44 (3.34)
95% CI of LS mean	(84.39, 98.48)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	0.69 (3.34)
95% CI of LS mean	(-6.35, 7.74)
Week 24	
n	18
Mean (SD)	90.51 (14.35)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	-0.23 (16.32)
Week 24 (MMRM)	
n	18
LS mean (SE)	90.51 (3.20)
95% CI of LS mean	(83.76, 97.26)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	-0.23 (3.20)
95% CI of LS mean	(-6.98, 6.52)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	0.23 (2.12)
95% CI of LS mean	(-4.25, 4.71)
P-value	0.9144

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	81.79 (19.20)
Week 4 (MMRM)	
n	27
LS mean (SE)	84.57 (2.45)
95% CI of LS mean	(79.53, 89.60)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	2.78 (2.45)
95% CI of LS mean	(-2.26, 7.81)
Week 8 (MMRM)	
n	27
LS mean (SE)	82.72 (2.98)
95% CI of LS mean	(76.60, 88.84)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	0.93 (2.98)
95% CI of LS mean	(-5.19, 7.05)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	85.79 (2.17)
95% CI of LS mean	(81.32, 90.26)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	4.00 (2.17)
95% CI of LS mean	(-0.47, 8.47)
Week 16 (MMRM)	
n	27
LS mean (SE)	83.33 (3.09)
95% CI of LS mean	(76.98, 89.68)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	1.54 (3.09)
95% CI of LS mean	(-4.81, 7.89)
Week 24	
n	27
Mean (SD)	85.49 (16.92)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	3.70 (14.68)
Week 24 (MMRM)	
n	27
LS mean (SE)	85.49 (2.43)
95% CI of LS mean	(80.50, 90.49)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	3.70 (2.43)
95% CI of LS mean	(-1.29, 8.70)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	2.62 (2.33)
95% CI of LS mean	(-2.19, 7.43)
P-value	0.2718

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	74.69 (17.06)
Week 4 (MMRM)	
n	27
LS mean (SE)	81.17 (2.53)
95% CI of LS mean	(75.96, 86.39)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	6.48 (2.53)
95% CI of LS mean	(1.27, 11.70)
Week 8 (MMRM)	
n	27
LS mean (SE)	80.56 (3.05)
95% CI of LS mean	(74.21, 86.90)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	5.86 (3.05)
95% CI of LS mean	(-0.48, 12.21)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	83.95 (2.45)
95% CI of LS mean	(78.91, 88.99)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	9.26 (2.45)
95% CI of LS mean	(4.22, 14.30)
Week 16 (MMRM)	
n	27
LS mean (SE)	84.26 (2.67)
95% CI of LS mean	(78.77, 89.75)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	9.57 (2.67)
95% CI of LS mean	(4.08, 15.06)
Week 24	
n	27
Mean (SD)	78.09 (15.01)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	3.40 (14.66)
Week 24 (MMRM)	
n	27
LS mean (SE)	78.09 (2.42)
95% CI of LS mean	(73.10, 83.08)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	3.40 (2.42)
95% CI of LS mean	(-1.60, 8.39)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	6.48 (2.14)
95% CI of LS mean	(2.06, 10.90)
P-value	0.0059

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	76.85 (19.43)
Week 4 (MMRM)	
n	36
LS mean (SE)	82.64 (1.94)
95% CI of LS mean	(78.68, 86.59)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	5.79 (1.94)
95% CI of LS mean	(1.83, 9.74)
Week 8 (MMRM)	
n	36
LS mean (SE)	80.32 (2.80)
95% CI of LS mean	(74.63, 86.02)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	3.47 (2.80)
95% CI of LS mean	(-2.22, 9.16)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	84.95 (1.94)
95% CI of LS mean	(81.00, 88.91)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	8.10 (1.94)
95% CI of LS mean	(4.15, 12.06)
Week 16 (MMRM)	
n	36
LS mean (SE)	84.49 (2.37)
95% CI of LS mean	(79.67, 89.31)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	7.64 (2.37)
95% CI of LS mean	(2.82, 12.46)
Week 24	
n	36
Mean (SD)	82.41 (16.64)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	5.56 (13.66)
Week 24 (MMRM)	
n	36
LS mean (SE)	82.41 (1.93)
95% CI of LS mean	(78.48, 86.33)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	5.56 (1.93)
95% CI of LS mean	(1.63, 9.48)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	6.60 (1.97)
95% CI of LS mean	(2.59, 10.61)
P-value	0.0020

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	81.02 (16.12)
Week 4 (MMRM)	
n	18
LS mean (SE)	83.33 (3.90)
95% CI of LS mean	(75.09, 91.58)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	2.31 (3.90)
95% CI of LS mean	(-5.93, 10.56)
Week 8 (MMRM)	
n	18
LS mean (SE)	84.26 (2.53)
95% CI of LS mean	(78.73, 89.79)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	3.24 (2.53)
95% CI of LS mean	(-2.29, 8.77)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	85.34 (3.09)
95% CI of LS mean	(78.73, 91.96)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	4.33 (3.09)
95% CI of LS mean	(-2.29, 10.95)
Week 16 (MMRM)	
n	18
LS mean (SE)	82.41 (3.83)
95% CI of LS mean	(74.27, 90.55)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	1.39 (3.83)
95% CI of LS mean	(-6.75, 9.53)
Week 24	
n	18
Mean (SD)	80.56 (15.91)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	-0.46 (15.78)
Week 24 (MMRM)	
n	18
LS mean (SE)	80.56 (3.25)
95% CI of LS mean	(73.69, 87.42)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	-0.46 (3.25)
95% CI of LS mean	(-7.33, 6.40)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	0.46 (2.35)
95% CI of LS mean	(-4.59, 5.51)
P-value	0.8468

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	74.07 (20.90)
Week 4 (MMRM)	
n	27
LS mean (SE)	81.89 (2.14)
95% CI of LS mean	(77.42, 86.36)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	7.82 (2.14)
95% CI of LS mean	(3.35, 12.29)
Week 8 (MMRM)	
n	27
LS mean (SE)	86.42 (3.58)
95% CI of LS mean	(78.99, 93.85)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	12.35 (3.58)
95% CI of LS mean	(4.92, 19.78)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	82.93 (3.45)
95% CI of LS mean	(75.82, 90.04)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	8.86 (3.45)
95% CI of LS mean	(1.74, 15.97)
Week 16 (MMRM)	
n	27
LS mean (SE)	82.30 (2.85)
95% CI of LS mean	(76.42, 88.19)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	8.23 (2.85)
95% CI of LS mean	(2.34, 14.12)
Week 24	
n	27
Mean (SD)	86.83 (14.79)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	12.76 (21.73)
Week 24 (MMRM)	
n	27
LS mean (SE)	86.83 (3.49)
95% CI of LS mean	(79.52, 94.14)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	12.76 (3.49)
95% CI of LS mean	(5.44, 20.07)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	10.49 (2.67)
95% CI of LS mean	(4.87, 16.12)
P-value	0.0010

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	66.67 (19.00)
Week 4 (MMRM)	
n	27
LS mean (SE)	74.49 (2.64)
95% CI of LS mean	(69.04, 79.93)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	7.82 (2.64)
95% CI of LS mean	(2.38, 13.26)
Week 8 (MMRM)	
n	27
LS mean (SE)	72.43 (3.63)
95% CI of LS mean	(64.95, 79.91)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	5.76 (3.63)
95% CI of LS mean	(-1.72, 13.24)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	72.02 (3.69)
95% CI of LS mean	(64.44, 79.60)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	5.35 (3.69)
95% CI of LS mean	(-2.23, 12.93)
Week 16 (MMRM)	
n	27
LS mean (SE)	74.07 (2.89)
95% CI of LS mean	(68.13, 80.02)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	7.41 (2.89)
95% CI of LS mean	(1.46, 13.36)
Week 24	
n	27
Mean (SD)	74.07 (20.90)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	7.41 (16.88)
Week 24 (MMRM)	
n	27
LS mean (SE)	74.07 (3.11)
95% CI of LS mean	(67.68, 80.47)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	7.41 (3.11)
95% CI of LS mean	(1.01, 13.80)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	7.41 (2.72)
95% CI of LS mean	(1.80, 13.02)
P-value	0.0117

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	70.37 (21.25)
Week 4 (MMRM)	
n	36
LS mean (SE)	77.16 (2.09)
95% CI of LS mean	(72.91, 81.41)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	6.79 (2.09)
95% CI of LS mean	(2.54, 11.04)
Week 8 (MMRM)	
n	36
LS mean (SE)	79.01 (3.12)
95% CI of LS mean	(72.68, 85.35)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	8.64 (3.12)
95% CI of LS mean	(2.31, 14.98)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	75.00 (2.97)
95% CI of LS mean	(68.97, 81.03)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	4.63 (2.97)
95% CI of LS mean	(-1.40, 10.66)
Week 16 (MMRM)	
n	36
LS mean (SE)	80.86 (2.46)
95% CI of LS mean	(75.87, 85.86)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	10.49 (2.46)
95% CI of LS mean	(5.50, 15.49)
Week 24	
n	36
Mean (SD)	79.94 (19.12)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	9.57 (19.73)
Week 24 (MMRM)	
n	36
LS mean (SE)	79.94 (2.78)
95% CI of LS mean	(74.29, 85.59)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	9.57 (2.78)
95% CI of LS mean	(3.91, 15.22)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	10.03 (2.34)
95% CI of LS mean	(5.26, 14.80)
P-value	0.0002

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	70.37 (18.28)
Week 4 (MMRM)	
n	18
LS mean (SE)	80.25 (2.71)
95% CI of LS mean	(74.50, 86.00)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	9.88 (2.71)
95% CI of LS mean	(4.13, 15.63)
Week 8 (MMRM)	
n	18
LS mean (SE)	80.25 (4.82)
95% CI of LS mean	(70.01, 90.48)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	9.88 (4.82)
95% CI of LS mean	(-0.36, 20.11)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	82.96 (4.80)
95% CI of LS mean	(72.80, 93.12)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	12.59 (4.80)
95% CI of LS mean	(2.43, 22.75)
Week 16 (MMRM)	
n	18
LS mean (SE)	72.84 (2.95)
95% CI of LS mean	(66.60, 79.08)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	2.47 (2.95)
95% CI of LS mean	(-3.77, 8.71)
Week 24	
n	18
Mean (SD)	81.48 (19.43)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	11.11 (19.43)
Week 24 (MMRM)	
n	18
LS mean (SE)	81.48 (4.57)
95% CI of LS mean	(71.75, 91.22)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	11.11 (4.57)
95% CI of LS mean	(1.38, 20.85)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	6.79 (3.26)
95% CI of LS mean	(-0.19, 13.77)
P-value	0.0559

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	77.78 (11.84)
Week 4 (MMRM)	
n	27
LS mean (SE)	74.07 (1.98)
95% CI of LS mean	(69.99, 78.16)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-3.70 (1.98)
95% CI of LS mean	(-7.78, 0.38)
Week 8 (MMRM)	
n	27
LS mean (SE)	75.06 (2.23)
95% CI of LS mean	(70.47, 79.65)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	-2.72 (2.23)
95% CI of LS mean	(-7.30, 1.87)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	77.84 (1.56)
95% CI of LS mean	(74.63, 81.06)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	0.07 (1.56)
95% CI of LS mean	(-3.14, 3.28)
Week 16 (MMRM)	
n	27
LS mean (SE)	79.26 (1.84)
95% CI of LS mean	(75.47, 83.05)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	1.48 (1.84)
95% CI of LS mean	(-2.30, 5.27)
Week 24	
n	27
Mean (SD)	79.01 (12.90)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	1.23 (13.47)
Week 24 (MMRM)	
n	27
LS mean (SE)	79.01 (2.30)
95% CI of LS mean	(74.28, 83.74)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	1.23 (2.30)
95% CI of LS mean	(-3.50, 5.97)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	1.36 (1.66)
95% CI of LS mean	(-2.05, 4.76)
P-value	0.4196

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	73.09 (12.47)
Week 4 (MMRM)	
n	27
LS mean (SE)	72.10 (2.74)
95% CI of LS mean	(66.47, 77.73)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-0.99 (2.74)
95% CI of LS mean	(-6.62, 4.64)
Week 8 (MMRM)	
n	27
LS mean (SE)	71.36 (1.59)
95% CI of LS mean	(68.08, 74.64)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	-1.73 (1.59)
95% CI of LS mean	(-5.01, 1.55)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	74.81 (2.45)
95% CI of LS mean	(69.77, 79.86)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	1.73 (2.45)
95% CI of LS mean	(-3.32, 6.77)
Week 16 (MMRM)	
n	27
LS mean (SE)	75.56 (1.99)
95% CI of LS mean	(71.46, 79.65)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	2.47 (1.99)
95% CI of LS mean	(-1.62, 6.56)
Week 24	
n	27
Mean (SD)	70.62 (13.11)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	-2.47 (15.92)
Week 24 (MMRM)	
n	27
LS mean (SE)	70.62 (2.62)
95% CI of LS mean	(65.21, 76.02)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	-2.47 (2.62)
95% CI of LS mean	(-7.87, 2.93)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	0.00 (1.96)
95% CI of LS mean	(-4.04, 4.04)
P-value	>0.9999

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	74.63 (13.41)
Week 4 (MMRM)	
n	36
LS mean (SE)	74.07 (2.16)
95% CI of LS mean	(69.69, 78.46)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	-0.56 (2.16)
95% CI of LS mean	(-4.94, 3.83)
Week 8 (MMRM)	
n	36
LS mean (SE)	73.15 (1.65)
95% CI of LS mean	(69.79, 76.50)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	-1.48 (1.65)
95% CI of LS mean	(-4.84, 1.87)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	75.37 (1.68)
95% CI of LS mean	(71.97, 78.77)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	0.74 (1.68)
95% CI of LS mean	(-2.66, 4.14)
Week 16 (MMRM)	
n	36
LS mean (SE)	77.96 (1.41)
95% CI of LS mean	(75.09, 80.83)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	3.33 (1.41)
95% CI of LS mean	(0.46, 6.20)
Week 24	
n	36
Mean (SD)	75.00 (12.28)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	0.37 (12.24)
Week 24 (MMRM)	
n	36
LS mean (SE)	75.00 (1.72)
95% CI of LS mean	(71.51, 78.49)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	0.37 (1.72)
95% CI of LS mean	(-3.12, 3.86)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	1.85 (1.26)
95% CI of LS mean	(-0.71, 4.41)
P-value	0.1509

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	77.04 (9.76)
Week 4 (MMRM)	
n	18
LS mean (SE)	71.11 (2.50)
95% CI of LS mean	(65.82, 76.40)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	-5.93 (2.50)
95% CI of LS mean	(-11.21, -0.64)
Week 8 (MMRM)	
n	18
LS mean (SE)	73.33 (2.40)
95% CI of LS mean	(68.26, 78.41)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	-3.70 (2.40)
95% CI of LS mean	(-8.78, 1.37)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	78.51 (2.83)
95% CI of LS mean	(72.52, 84.50)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	1.47 (2.83)
95% CI of LS mean	(-4.52, 7.46)
Week 16 (MMRM)	
n	18
LS mean (SE)	76.30 (2.82)
95% CI of LS mean	(70.30, 82.29)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	-0.74 (2.82)
95% CI of LS mean	(-6.74, 5.26)
Week 24	
n	18
Mean (SD)	74.44 (16.21)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	-2.59 (19.01)
Week 24 (MMRM)	
n	18
LS mean (SE)	74.44 (4.18)
95% CI of LS mean	(65.56, 83.33)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	-2.59 (4.18)
95% CI of LS mean	(-11.48, 6.30)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-1.67 (2.98)
95% CI of LS mean	(-7.97, 4.64)
P-value	0.5834

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	72.84 (34.64)
Week 4 (MMRM)	
n	27
LS mean (SE)	69.14 (4.86)
95% CI of LS mean	(59.15, 79.12)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-3.70 (4.86)
95% CI of LS mean	(-13.69, 6.29)
Week 8 (MMRM)	
n	27
LS mean (SE)	79.01 (4.44)
95% CI of LS mean	(69.85, 88.18)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	6.17 (4.44)
95% CI of LS mean	(-2.99, 15.34)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	74.08 (3.95)
95% CI of LS mean	(65.96, 82.20)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	1.24 (3.95)
95% CI of LS mean	(-6.88, 9.36)
Week 16 (MMRM)	
n	27
LS mean (SE)	76.54 (3.91)
95% CI of LS mean	(68.50, 84.58)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	3.70 (3.91)
95% CI of LS mean	(-4.34, 11.74)
Week 24	
n	27
Mean (SD)	71.60 (31.63)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	-1.23 (21.64)
Week 24 (MMRM)	
n	27
LS mean (SE)	71.60 (3.77)
95% CI of LS mean	(63.85, 79.36)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	-1.23 (3.77)
95% CI of LS mean	(-8.99, 6.52)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	1.23 (2.80)
95% CI of LS mean	(-4.54, 7.01)
P-value	0.6635

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	70.37 (37.36)
Week 4 (MMRM)	
n	27
LS mean (SE)	71.60 (5.39)
95% CI of LS mean	(60.52, 82.69)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	1.23 (5.39)
95% CI of LS mean	(-9.85, 12.32)
Week 8 (MMRM)	
n	27
LS mean (SE)	75.31 (4.76)
95% CI of LS mean	(65.50, 85.11)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	4.94 (4.76)
95% CI of LS mean	(-4.87, 14.74)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	76.54 (4.73)
95% CI of LS mean	(66.80, 86.29)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	6.17 (4.73)
95% CI of LS mean	(-3.57, 15.92)
Week 16 (MMRM)	
n	27
LS mean (SE)	79.01 (4.52)
95% CI of LS mean	(69.71, 88.32)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	8.64 (4.52)
95% CI of LS mean	(-0.66, 17.95)
Week 24	
n	27
Mean (SD)	81.48 (29.72)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	11.11 (36.98)
Week 24 (MMRM)	
n	27
LS mean (SE)	81.48 (5.37)
95% CI of LS mean	(70.41, 92.55)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	11.11 (5.37)
95% CI of LS mean	(0.04, 22.18)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	9.88 (4.56)
95% CI of LS mean	(0.49, 19.26)
P-value	0.0399

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	71.30 (37.50)
Week 4 (MMRM)	
n	36
LS mean (SE)	70.37 (5.00)
95% CI of LS mean	(60.21, 80.53)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	-0.93 (5.00)
95% CI of LS mean	(-11.09, 9.24)
Week 8 (MMRM)	
n	36
LS mean (SE)	78.70 (4.01)
95% CI of LS mean	(70.55, 86.85)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	7.41 (4.01)
95% CI of LS mean	(-0.74, 15.56)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	76.85 (3.85)
95% CI of LS mean	(69.03, 84.68)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	5.56 (3.85)
95% CI of LS mean	(-2.27, 13.38)
Week 16 (MMRM)	
n	36
LS mean (SE)	81.48 (3.70)
95% CI of LS mean	(73.97, 89.00)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	10.19 (3.70)
95% CI of LS mean	(2.67, 17.70)
Week 24	
n	36
Mean (SD)	80.56 (28.03)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	9.26 (31.48)
Week 24 (MMRM)	
n	36
LS mean (SE)	80.56 (3.88)
95% CI of LS mean	(72.68, 88.43)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	9.26 (3.88)
95% CI of LS mean	(1.38, 17.14)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	9.72 (3.12)
95% CI of LS mean	(3.38, 16.06)
P-value	0.0037

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	72.22 (32.84)
Week 4 (MMRM)	
n	18
LS mean (SE)	70.37 (3.41)
95% CI of LS mean	(63.12, 77.62)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	-1.85 (3.41)
95% CI of LS mean	(-9.11, 5.40)
Week 8 (MMRM)	
n	18
LS mean (SE)	74.07 (5.24)
95% CI of LS mean	(62.94, 85.21)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	1.85 (5.24)
95% CI of LS mean	(-9.28, 12.99)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	72.34 (5.28)
95% CI of LS mean	(61.19, 83.49)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	0.12 (5.28)
95% CI of LS mean	(-11.03, 11.27)
Week 16 (MMRM)	
n	18
LS mean (SE)	70.37 (4.66)
95% CI of LS mean	(60.50, 80.25)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	-1.85 (4.66)
95% CI of LS mean	(-11.73, 8.02)
Week 24	
n	18
Mean (SD)	68.52 (35.19)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	-3.70 (27.75)
Week 24 (MMRM)	
n	18
LS mean (SE)	68.52 (6.28)
95% CI of LS mean	(55.25, 81.79)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	-3.70 (6.28)
95% CI of LS mean	(-16.97, 9.56)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-2.78 (4.93)
95% CI of LS mean	(-13.21, 7.65)
P-value	0.5806

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 2.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period non-(F/MF)
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Any Pulmonary Exacerbation	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 2.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period non-(F/MF)
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Pulmonary Exacerbation Requiring Hospitalization	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 2.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period non-(F/MF)
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Pulmonary Exacerbation Requiring IV Antibiotic Therapy	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 2.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period non-(F/MF)
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Pulmonary Exacerbation Requiring Hospitalization or IV Antibiotic Therapy	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 2.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

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Table 2.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

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Table 2.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

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Table 2.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 18

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

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Table 2.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

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Table 2.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 2.2.2.14.1
Study VX21-121-105: Subgroup Factor Test for
Time-to-First Pulmonary Exacerbation during the PEx Analysis Period non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Log-rank test.

Table 2.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 2.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 18 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 2.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 2.2.2.15.1
Study VX21-121-105: Subgroup Factor Test for
Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Log-rank test.

Table 2.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 2.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 2.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 2.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 18 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 2.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 2.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 2.2.2.16.1
Study VX21-121-105: Subgroup Factor Test for
Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Log-rank test.

Table 2.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 2.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 18 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 2.3.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 54 n (%)
Subjects with any TEAEs	50 (92.59)
Respiratory, thoracic and mediastinal disorders	34 (62.96)
Cough	25 (46.30)
Oropharyngeal pain	10 (18.52)
Rhinorrhoea	9 (16.67)
Infections and infestations	22 (40.74)
Gastrointestinal disorders	17 (31.48)
Abdominal pain	8 (14.81)
Vomiting	6 (11.11)
Investigations	16 (29.63)
General disorders and administration site conditions	15 (27.78)
Pyrexia	12 (22.22)
Nervous system disorders	13 (24.07)
Headache	11 (20.37)
Injury, poisoning and procedural complications	8 (14.81)
Skin and subcutaneous tissue disorders	7 (12.96)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 54 n (%)
Subjects with any TEAEs	50 (92.59)
Grade 1/Mild	32 (59.26)
Grade 2/Moderate	18 (33.33)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Respiratory, thoracic and mediastinal disorders	34 (62.96)
Grade 1/Mild	27 (50.00)
Grade 2/Moderate	7 (12.96)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Cough	25 (46.30)
Grade 1/Mild	20 (37.04)
Grade 2/Moderate	5 (9.26)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Oropharyngeal pain	10 (18.52)
Grade 1/Mild	10 (18.52)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 54 n (%)
Rhinorrhoea	9 (16.67)
Grade 1/Mild	9 (16.67)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0
Infections and infestations	22 (40.74)
Grade 1/Mild	15 (27.78)
Grade 2/Moderate	7 (12.96)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Gastrointestinal disorders	17 (31.48)
Grade 1/Mild	15 (27.78)
Grade 2/Moderate	2 (3.70)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Abdominal pain	8 (14.81)
Grade 1/Mild	7 (12.96)
Grade 2/Moderate	1 (1.85)
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 54 n (%)
Vomiting	6 (11.11)
Grade 1/Mild	4 (7.41)
Grade 2/Moderate	2 (3.70)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Investigations	16 (29.63)
Grade 1/Mild	12 (22.22)
Grade 2/Moderate	4 (7.41)
Grade 3/Severe	0
Grade 4/Life Threatening	0
General disorders and administration site conditions	15 (27.78)
Grade 1/Mild	13 (24.07)
Grade 2/Moderate	2 (3.70)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Pyrexia	12 (22.22)
Grade 1/Mild	10 (18.52)
Grade 2/Moderate	2 (3.70)
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 54 n (%)
Nervous system disorders	13 (24.07)
Grade 1/Mild	9 (16.67)
Grade 2/Moderate	4 (7.41)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Headache	11 (20.37)
Grade 1/Mild	9 (16.67)
Grade 2/Moderate	2 (3.70)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Injury, poisoning and procedural complications	8 (14.81)
Grade 1/Mild	8 (14.81)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0
Skin and subcutaneous tissue disorders	7 (12.96)
Grade 1/Mild	7 (12.96)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.1.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 54 n (%)

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 5% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

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Table 2.3.1.3
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 54 n (%)
Subjects with any Serious TEAEs	4 (7.41)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 5% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.1.4
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 54 n (%)
Subjects with any TEAEs leading to treatment discontinuation	1 (1.85)
General disorders and administration site conditions	1 (1.85)
Fatigue	1 (1.85)
Respiratory, thoracic and mediastinal disorders	1 (1.85)
Cough	1 (1.85)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.1.5
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events - Total and by Severity non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	4 (7.41)
Subjects with non-severe events (Maximum Grade 1/2)	4 (7.41)
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 2.3.1.6
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events - Total and by Severity non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	1 (1.85)
Subjects with non-severe events (Maximum Grade 1/2)	1 (1.85)
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 2.3.1.7
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events - Total and by Severity non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Subjects with any Treatment-emergent Rash Events	4 (7.41)
Subjects with non-severe events (Maximum Grade 1/2)	4 (7.41)
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 2.3.1.8
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events - Total and by Severity non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Subjects with any Treatment-emergent Cataract Events	1 (1.85)
Subjects with non-severe events (Maximum Grade 1/2)	1 (1.85)
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 2.3.1.9
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events - Total and by Severity non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	0
Subjects with non-severe events (Maximum Grade 1/2)	0
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 2.3.1.10
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events - Total and by Severity non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	3 (5.56)
Subjects with non-severe events (Maximum Grade 1/2)	3 (5.56)
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 2.3.1.11
Study VX21-121-105: Summary of Death non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)

No data met the criteria for this table.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.

Table 2.3.1.12
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	10 (18.52)
Subjects with non-severe events (Maximum Grade 1/2)	10 (18.52)
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	2 (3.70)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 2.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
Subjects with any TEAEs	
Sex (Male vs. Female)	>0.9999
Region (North America vs. Rest of the World)	0.1416
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-
Respiratory, thoracic and mediastinal disorders	
Sex (Male vs. Female)	0.5730
Region (North America vs. Rest of the World)	0.6902
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
Cough	
Sex (Male vs. Female)	0.7849
Region (North America vs. Rest of the World)	0.4402
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-
Infections and infestations	
Sex (Male vs. Female)	0.2679
Region (North America vs. Rest of the World)	0.6953
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
Investigations	
Sex (Male vs. Female)	0.0738
Region (North America vs. Rest of the World)	0.6734
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-
General disorders and administration site conditions	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	>0.9999
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 27 n (%)
Subjects with any TEAEs	25 (92.59)
Respiratory, thoracic and mediastinal disorders	18 (66.67)
Cough	12 (44.44)
Infections and infestations	13 (48.15)
Investigations	11 (40.74)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 27 n (%)
Subjects with any TEAEs	25 (92.59)
Respiratory, thoracic and mediastinal disorders	16 (59.26)
Cough	13 (48.15)
Infections and infestations	9 (33.33)
Investigations	5 (18.52)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 36 n (%)
Subjects with any TEAEs	32 (88.89)
Respiratory, thoracic and mediastinal disorders	22 (61.11)
Cough	18 (50.00)
Infections and infestations	14 (38.89)
General disorders and administration site conditions	10 (27.78)
Investigations	10 (27.78)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 18 n (%)
Subjects with any TEAEs	18 (100.00)
Respiratory, thoracic and mediastinal disorders	12 (66.67)
Cough	7 (38.89)
Infections and infestations	8 (44.44)
Investigations	6 (33.33)
General disorders and administration site conditions	5 (27.78)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 4 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.2.1
Study VX21-121-105: Subgroup Factor Test for Grade 3/4/5 TEAEs by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

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Table 2.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

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Table 2.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

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Table 2.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

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Table 2.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 18 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 4 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

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Table 2.3.2.3.1
Study VX21-121-105: Subgroup Factor Test for Serious TEAEs by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

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Table 2.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 18 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 4 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

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Table 2.3.2.4.1
Study VX21-121-105: Subgroup Factor Test for TEAEs Leading to Treatment Discontinuation by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 18 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 4 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

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Table 2.3.2.5.1
Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Elevated Transaminase Events non-(F/MF)
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.5.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.5.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.5.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.5.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 18 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.5.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.5.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 2.3.2.6.1
Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Creatine Kinase Events non-(F/MF)
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.6.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.6.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.6.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 36 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.6.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 18 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.6.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.6.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 2.3.2.7.1
Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Rash Events non-(F/MF)
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.7.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.7.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.7.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.7.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 18 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 2.3.2.7.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.7.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 2.3.2.8.1
Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Cataract Events non-(F/MF)
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.8.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.8.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.8.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.8.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 18 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.8.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.8.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 2.3.2.9.1
Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Hypoglycemia Events non-(F/MF)
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.9.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.9.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.9.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.9.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 18 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.9.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.9.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.10.1
Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Neuropsychiatric Events non-(F/MF)
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.10.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.10.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.10.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.10.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 18 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.10.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.10.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 2.3.2.11.1
Study VX21-121-105: Subgroup Factor Test for Death non-(F/MF)
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 18 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 2.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.12.1
Study VX21-121-105: Subgroup Factor Test for Treatment-emergent Infective Pulmonary Exacerbation Events non-(F/MF)
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 36 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 18 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 2.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 3.1.1.1
Study VX21-121-105: Summary of Duration of Observation (Weeks) per Endpoint
Full Analysis Set

Duration of observation (weeks)	VNZ/TEZ/D-IVA N = 78
Overall Study Observation Time	
n	78
Mean (SD)	24.15 (0.48)
Median	24.14
Min, Max	23.14, 25.57
$ppFEV_1$ (percentage points)	
n	77
Mean (SD)	23.30 (2.74)
Median	24.14
Min, Max	12.00, 25.57
BMI (kg/m^2)	
n	78
Mean (SD)	24.15 (0.48)
Median	24.14
Min, Max	23.14, 25.57
BMI z-score	
n	78
Mean (SD)	24.15 (0.48)
Median	24.14
Min, Max	23.14, 25.57
Sweat Chloride (mmol/L)	
n	78
Mean (SD)	23.74 (1.83)
Median	24.14
Min, Max	16.14, 25.57

- Observation duration [weeks] is defined as (date of last observation - first date of study drug in the Treatment Period +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results. For $LCI_{2.5}$, observation duration is derived from dates of accepted multiple breath washout results.

Table 3.1.1.1
Study VX21-121-105: Summary of Duration of Observation (Weeks) per Endpoint
Full Analysis Set

Duration of observation (weeks)	VNZ/TEZ/D-IVA N = 78
Weight (kg)	
n	78
Mean (SD)	24.15 (0.48)
Median	24.14
Min, Max	23.14, 25.57
Weight z-score	
n	78
Mean (SD)	24.15 (0.48)
Median	24.14
Min, Max	23.14, 25.57
Height (cm)	
n	78
Mean (SD)	24.15 (0.48)
Median	24.14
Min, Max	23.14, 25.57
Height z-score	
n	78
Mean (SD)	24.15 (0.48)
Median	24.14
Min, Max	23.14, 25.57
CFQ-R	
n	78
Mean (SD)	24.15 (0.48)
Median	24.14
Min, Max	23.14, 25.57

- Observation duration [weeks] is defined as (date of last observation - first date of study drug in the Treatment Period +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results. For $LCI_{2.5}$, observation duration is derived from dates of accepted multiple breath washout results.

Table 3.1.1.1
Study VX21-121-105: Summary of Duration of Observation (Weeks) per Endpoint
Full Analysis Set

Duration of observation (weeks)	VNZ/TEZ/D-IVA N = 78
Pulmonary Exacerbation	
n	78
Mean (SD)	24.15 (0.48)
Median	24.14
Min, Max	23.14, 25.57
$LCI_{2.5}$	
n	76
Mean (SD)	22.19 (5.01)
Median	24.14
Min, Max	3.86, 25.57
Safety	
n	78
Mean (SD)	23.98 (1.64)
Median	24.14
Min, Max	10.29, 25.57

- Observation duration [weeks] is defined as (date of last observation - first date of study drug in the Treatment Period +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results. For $LCI_{2.5}$, observation duration is derived from dates of accepted multiple breath washout results.

Table 3.1.2.1
Study VX21-121-105: Summary of Patients with Ongoing Antibiotic Medications at Baseline or at Week 24
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline, N1	78
Subjects with 0 ongoing AB	63 (80.77)
Subjects with 1 ongoing AB	12 (15.38)
Subjects with ≥ 2 ongoing AB	3 (3.85)
Subjects with ≥ 1 ongoing IV AB	0
Week 24, N1	78
Subjects with 0 ongoing AB	66 (84.62)
Subjects with 1 ongoing AB	10 (12.82)
Subjects with ≥ 2 ongoing AB	2 (2.56)
Subjects with ≥ 1 ongoing IV AB	0

- AB: Antibiotic medications are defined as those medications with the ATC level 2 names of "ANTIBACTERIALS FOR SYSTEMIC USE" and "ANTIMYCOBACTERIALS".
- Antibiotic medications included in this summary refer to those with route being "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- IV antibiotic medications refer to those with route being "INTRAVENOUS" or "INTRAVENOUS BOLUS".
- The ongoing antibiotic medications at baseline refer to those with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing antibiotic medications at Week 24 refer to those with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 3.1.2.2
Study VX21-121-105: Summary of Patients with Antibiotic Medications during the Study Treatment Period
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
All subjects	78
Subjects with 0 AB	27 (34.62)
Subjects with 1-3 AB	44 (56.41)
Subjects with ≥ 4 AB	7 (8.97)
Subjects with 0 IV AB	73 (93.59)
Subjects with 1 IV AB	3 (3.85)
Subjects with ≥ 2 IV AB	2 (2.56)
Subjects with 0 ongoing antibiotic medication at baseline	63
Subjects with 0 AB	27 (42.86)
Subjects with 1-3 AB	34 (53.97)
Subjects with ≥ 4 AB	2 (3.17)
Subjects with 0 IV AB	59 (93.65)
Subjects with 1 IV AB	3 (4.76)
Subjects with ≥ 2 IV AB	1 (1.59)

- AB: Antibiotic medications are defined as those medications with the ATC level 2 names of "ANTIBACTERIALS FOR SYSTEMIC USE" and "ANTIMYCOBACTERIALS".
- Antibiotic medications included in this summary refer to those with route being "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- IV antibiotic medications refer to those with route being "INTRAVENOUS" or "INTRAVENOUS BOLUS".
- Antibiotic medications during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period, and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 3.1.3.1
Study VX21-121-105: Summary of Patients with Ongoing Physiotherapies at Baseline or at Week 24
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline, N1	78
Subjects with 0 ongoing PT	21 (26.92)
Subjects with 1 ongoing PT	50 (64.10)
Subjects with ≥ 2 ongoing PT	7 (8.97)
Week 24, N1	78
Subjects with 0 ongoing PT	21 (26.92)
Subjects with 1 ongoing PT	49 (62.82)
Subjects with ≥ 2 ongoing PT	8 (10.26)

- PT: Physiotherapies refer to the non-pharmacological treatments with preferred names of "Positive expiratory pressure therapy", "Airway secretion clearance therapy", "Positive end-expiratory pressure", or "Physiotherapy chest".
- The ongoing physiotherapy at baseline is defined as a physiotherapy whose start date is prior to first dose date of study drug in the Treatment Period and the end date is ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing physiotherapy at Week 24 is defined as a physiotherapy whose start date is prior to Week 24 visit date and the end date is ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 3.1.3.2
Study VX21-121-105: Summary of Patients with Physiotherapies during the Study Treatment Period
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
All subjects	78
Subjects with 0 PT	21 (26.92)
Subjects with 1 PT	49 (62.82)
Subjects with ≥ 2 PT	8 (10.26)
Subjects with 0 ongoing physiotherapies at baseline	21
Subjects with 0 PT	21 (100.00)
Subjects with 1 PT	0
Subjects with ≥ 2 PT	0

- PT: Physiotherapies refer to the non-pharmacological treatments with preferred names of "Positive expiratory pressure therapy", "Airway secretion clearance therapy", "Positive end-expiratory pressure", or "Physiotherapy chest".
- Physiotherapies during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period, and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 3.1.4.1
Study VX21-121-105: Summary of Patients with Ongoing Inhaled Medications at Baseline or at Week 24
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline, N1	78
Subjects with 0 ongoing IM	6 (7.69)
Subjects with 1 ongoing IM	6 (7.69)
Subjects with ≥ 2 ongoing IM	66 (84.62)
Week 24, N1	78
Subjects with 0 ongoing IM	6 (7.69)
Subjects with 1 ongoing IM	6 (7.69)
Subjects with ≥ 2 ongoing IM	66 (84.62)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB) and for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 24 refer to those IMs with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 3.1.4.2
Study VX21-121-105: Summary of Patients with Inhaled Medications during the Study Treatment Period
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
All subjects	78
Subjects with 0 IM	5 (6.41)
Subjects with 1 IM	6 (7.69)
Subjects with ≥ 2 IM	67 (85.90)
Subjects with 0 ongoing inhaled medication at baseline	6
Subjects with 0 IM	5 (83.33)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	1 (16.67)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB) and for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 3.1.4.3
Study VX21-121-105: Summary of Patients with Ongoing Inhaled Medications for Mucolytics at Baseline or at Week 24
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline, N1	78
Subjects with 0 ongoing IM	11 (14.10)
Subjects with 1 ongoing IM	26 (33.33)
Subjects with ≥ 2 ongoing IM	41 (52.56)
Week 24, N1	78
Subjects with 0 ongoing IM	11 (14.10)
Subjects with 1 ongoing IM	26 (33.33)
Subjects with ≥ 2 ongoing IM	41 (52.56)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 24 refer to those IMs with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 3.1.4.4
Study VX21-121-105: Summary of Patients with Inhaled Medications for Mucolytics during the Study Treatment Period
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
All subjects	78
Subjects with 0 IM	11 (14.10)
Subjects with 1 IM	26 (33.33)
Subjects with ≥ 2 IM	41 (52.56)
Subjects with 0 ongoing inhaled medication at baseline	11
Subjects with 0 IM	11 (100.00)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	0

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 3.1.4.5
Study VX21-121-105: Summary of Patients with Ongoing Inhaled Medications for Obstructive Airway Disease at Baseline or at Week 24
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline, N1	78
Subjects with 0 ongoing IM	18 (23.08)
Subjects with 1 ongoing IM	35 (44.87)
Subjects with ≥ 2 ongoing IM	25 (32.05)
Week 24, N1	78
Subjects with 0 ongoing IM	18 (23.08)
Subjects with 1 ongoing IM	35 (44.87)
Subjects with ≥ 2 ongoing IM	25 (32.05)

- IM: Inhaled medications refer to those medications for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 24 refer to those IMs with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 3.1.4.6
Study VX21-121-105: Summary of Patients with Inhaled Medications for Obstructive Airway Disease during the Study Treatment Period
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
All subjects	78
Subjects with 0 IM	17 (21.79)
Subjects with 1 IM	34 (43.59)
Subjects with ≥ 2 IM	27 (34.62)
Subjects with 0 ongoing inhaled medication at baseline	18
Subjects with 0 IM	17 (94.44)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	1 (5.56)

- IM: Inhaled medications refer to those medications for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing..
- The percentages in this table are calculated based on the number of subjects under each category.

Table 3.1.5.1
Study VX21-121-105: Summary of Patients with Ongoing CF-related Medications at Baseline or at Week 24
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline, N1	78
Subjects with 0 ongoing CF-related medications	1 (1.28)
Subjects with 1 ongoing CF-related medications	4 (5.13)
Subjects with 2 ongoing CF-related medications	2 (2.56)
Subjects with 3 ongoing CF-related medications	13 (16.67)
Subjects with 4 ongoing CF-related medications	16 (20.51)
Subjects with ≥5 ongoing CF-related medications	42 (53.85)
Week 24, N1	78
Subjects with 0 ongoing CF-related medications	1 (1.28)
Subjects with 1 ongoing CF-related medications	4 (5.13)
Subjects with 2 ongoing CF-related medications	4 (5.13)
Subjects with 3 ongoing CF-related medications	14 (17.95)
Subjects with 4 ongoing CF-related medications	15 (19.23)
Subjects with ≥5 ongoing CF-related medications	40 (51.28)

- CF-related medications: CF co-medications are defined as those medications with
o ATC level 2 names of "DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES", "DIGESTIVES, INCL. ENZYMES", "ANTIBACTERIALS FOR SYSTEMIC USE", "DRUGS USED IN DIABETES", "BILE AND LIVER THERAPY", "GENERAL NUTRIENTS";
o or ATC level 3 names of "DRUGS FOR CONSTIPATION", "PROPULSIVES";
o or ATC level 4 names of "MUCOLYTICS".
In addition, the route of administration for "DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES" and "MUCOLYTICS" requires to be "RESPIRATORY (INHALATION)" and the route for "ANTIBACTERIALS FOR SYSTEMIC USE" requires to be "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- The ongoing CF-related medications at baseline refer to those CF-related medications with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing CF-related medications at Week 24 refer to those CF-related medications with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 3.2.1.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	77
Mean (SD)	99.66 (15.07)
Week 24	
n	70
Mean (SD)	99.97 (13.56)
Absolute Change at Week 24	
n	69
Mean (SD)	-1.19 (8.45)
Absolute Change through Week 24 (MMRM)	
n	74
LS mean (SE)	-0.07 (0.99)
95% CI of LS mean	(-2.05, 1.90)
P-value	0.9421

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline ppFEV$_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	16.83 (2.13)
Week 24	
n	78
Mean (SD)	17.05 (2.43)
Absolute Change at Week 24	
n	78
Mean (SD)	0.22 (0.73)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	0.22 (0.08)
95% CI of LS mean	(0.05, 0.38)
P-value	0.0097

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.1.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	0.07 (0.87)
Week 24	
n	78
Mean (SD)	0.02 (0.96)
Absolute Change at Week 24	
n	78
Mean (SD)	-0.05 (0.31)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	-0.05 (0.03)
95% CI of LS mean	(-0.12, 0.02)
P-value	0.1533

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.1.4.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	77
Mean (SD)	40.41 (20.94)
Week 24	
n	74
Mean (SD)	32.14 (15.49)
Absolute Change at Week 24	
n	74
Mean (SD)	-8.72 (13.95)
Absolute Change through Week 24 (MMRM)	
n	77
LS mean (SE)	-8.65 (1.17)
95% CI of LS mean	(-10.98, -6.32)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit and genotype group (F/MF vs rest), with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.4.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Non-missing value at Week 24, N1	74
Number of subjects with missing value at Week 24	4
SwCl <60 mmol/L at Week 24, n (%)	69 (88.46)
95% CI for the proportion	(79.22, 94.59)

- N1: number of subjects with non-missing SwCl at Week 24
- n: number of subjects with SwCl <60 mmol/L
- 95% CI is based on the Clopper-Pearson method

Table 3.2.1.4.3
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Non-missing value at Week 24, N1	74
Number of subjects with missing value at Week 24	4
SwCl <30 mmol/L at Week 24, n (%)	38 (48.72)
95% CI for the proportion	(37.23, 60.31)

- N1: number of subjects with non-missing SwCl at Week 24
- n: number of subjects with SwCl <30 mmol/L
- 95% CI is based on the Clopper-Pearson method

Table 3.2.1.5
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	30.21 (7.48)
Week 24	
n	78
Mean (SD)	31.88 (8.21)
Absolute Change at Week 24	
n	78
Mean (SD)	1.67 (1.51)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	1.67 (0.17)
95% CI of LS mean	(1.34, 2.00)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.1.6
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	0.00 (0.89)
Week 24	
n	78
Mean (SD)	-0.01 (0.95)
Absolute Change at Week 24	
n	78
Mean (SD)	-0.02 (0.22)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	-0.02 (0.03)
95% CI of LS mean	(-0.07, 0.03)
P-value	0.4704

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.1.7
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	132.96 (10.51)
Week 24	
n	78
Mean (SD)	135.69 (10.71)
Absolute Change at Week 24	
n	78
Mean (SD)	2.73 (1.05)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	2.73 (0.12)
95% CI of LS mean	(2.50, 2.97)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.1.8
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	-0.03 (0.94)
Week 24	
n	78
Mean (SD)	-0.02 (0.96)
Absolute Change at Week 24	
n	78
Mean (SD)	0.01 (0.17)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	0.01 (0.02)
95% CI of LS mean	(-0.03, 0.05)
P-value	0.5430

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.1.9
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	72
Mean (SD)	6.63 (0.74)
Week 24	
n	61
Mean (SD)	6.46 (0.54)
Absolute Change at Week 24	
n	58
Mean (SD)	-0.17 (0.54)
Absolute Change through Week 24 (MMRM)	
n	58
LS mean (SE)	-0.09 (0.05)
95% CI of LS mean	(-0.19, 0.01)
P-value	0.0832

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 3.2.1.10.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	75
Mean (SD)	84.78 (16.12)
Week 4 (MMRM)	
n	75
LS mean (SE)	85.44 (1.70)
95% CI of LS mean	(82.05, 88.83)
Absolute Change at Week 4 (MMRM)	
n	75
LS mean (SE)	0.67 (1.70)
95% CI of LS mean	(-2.72, 4.06)
Week 8 (MMRM)	
n	75
LS mean (SE)	86.44 (1.74)
95% CI of LS mean	(82.97, 89.91)
Absolute Change at Week 8 (MMRM)	
n	75
LS mean (SE)	1.67 (1.74)
95% CI of LS mean	(-1.80, 5.14)
Week 12 (MMRM)	
n	74
LS mean (SE)	90.40 (1.31)
95% CI of LS mean	(87.79, 93.00)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 12 (MMRM)	
n	74
LS mean (SE)	5.62 (1.31)
95% CI of LS mean	(3.02, 8.23)
Week 16 (MMRM)	
n	75
LS mean (SE)	90.89 (1.34)
95% CI of LS mean	(88.22, 93.55)
Absolute Change at Week 16 (MMRM)	
n	75
LS mean (SE)	6.11 (1.34)
95% CI of LS mean	(3.45, 8.78)
Week 24	
n	78
Mean (SD)	85.79 (15.61)
Absolute Change at Week 24	
n	75
Mean (SD)	1.78 (18.70)
Week 24 (MMRM)	
n	78
LS mean (SE)	86.56 (1.66)
95% CI of LS mean	(83.25, 89.86)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24 (MMRM)	
n	75
LS mean (SE)	1.78 (1.66)
95% CI of LS mean	(-1.52, 5.08)
Absolute Change through Week 24 (MMRM)	
n	75
LS mean (SE)	3.94 (1.21)
95% CI of LS mean	(1.53, 6.36)
P-value	0.0017

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains)
Full Analysis Set

Domain: Respiration

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	75 (96.15)
Week 4	75 (96.15)
Absolute Change at Week 4	75 (96.15)
Week 8	75 (96.15)
Absolute Change at Week 8	75 (96.15)
Week 12	74 (94.87)
Absolute Change at Week 12	74 (94.87)
Week 16	75 (96.15)
Absolute Change at Week 16	75 (96.15)
Week 24	78 (100.00)
Absolute Change at Week 24	75 (96.15)
Through Week 24	78 (100.00)
Absolute Change through Week 24	75 (96.15)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains)
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	75 (96.15)
Week 4	75 (96.15)
Absolute Change at Week 4	75 (96.15)
Week 8	75 (96.15)
Absolute Change at Week 8	75 (96.15)
Week 12	74 (94.87)
Absolute Change at Week 12	74 (94.87)
Week 16	75 (96.15)
Absolute Change at Week 16	75 (96.15)
Week 24	78 (100.00)
Absolute Change at Week 24	75 (96.15)
Through Week 24	78 (100.00)
Absolute Change through Week 24	75 (96.15)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains)
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	74 (94.87)
Week 4	75 (96.15)
Absolute Change at Week 4	74 (94.87)
Week 8	75 (96.15)
Absolute Change at Week 8	74 (94.87)
Week 12	74 (94.87)
Absolute Change at Week 12	73 (93.59)
Week 16	75 (96.15)
Absolute Change at Week 16	74 (94.87)
Week 24	78 (100.00)
Absolute Change at Week 24	74 (94.87)
Through Week 24	78 (100.00)
Absolute Change through Week 24	74 (94.87)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains)
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	75 (96.15)
Week 4	75 (96.15)
Absolute Change at Week 4	75 (96.15)
Week 8	75 (96.15)
Absolute Change at Week 8	75 (96.15)
Week 12	74 (94.87)
Absolute Change at Week 12	74 (94.87)
Week 16	75 (96.15)
Absolute Change at Week 16	75 (96.15)
Week 24	78 (100.00)
Absolute Change at Week 24	75 (96.15)
Through Week 24	78 (100.00)
Absolute Change through Week 24	75 (96.15)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains)
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	75 (96.15)
Week 4	75 (96.15)
Absolute Change at Week 4	75 (96.15)
Week 8	75 (96.15)
Absolute Change at Week 8	75 (96.15)
Week 12	74 (94.87)
Absolute Change at Week 12	74 (94.87)
Week 16	75 (96.15)
Absolute Change at Week 16	75 (96.15)
Week 24	78 (100.00)
Absolute Change at Week 24	75 (96.15)
Through Week 24	78 (100.00)
Absolute Change through Week 24	75 (96.15)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains)
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	75 (96.15)
Week 4	75 (96.15)
Absolute Change at Week 4	75 (96.15)
Week 8	75 (96.15)
Absolute Change at Week 8	75 (96.15)
Week 12	74 (94.87)
Absolute Change at Week 12	74 (94.87)
Week 16	75 (96.15)
Absolute Change at Week 16	75 (96.15)
Week 24	78 (100.00)
Absolute Change at Week 24	75 (96.15)
Through Week 24	78 (100.00)
Absolute Change through Week 24	75 (96.15)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains)
Full Analysis Set

Domain: Social

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	75 (96.15)
Week 4	75 (96.15)
Absolute Change at Week 4	75 (96.15)
Week 8	75 (96.15)
Absolute Change at Week 8	75 (96.15)
Week 12	74 (94.87)
Absolute Change at Week 12	74 (94.87)
Week 16	75 (96.15)
Absolute Change at Week 16	75 (96.15)
Week 24	78 (100.00)
Absolute Change at Week 24	75 (96.15)
Through Week 24	78 (100.00)
Absolute Change through Week 24	75 (96.15)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains)
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	75 (96.15)
Week 4	75 (96.15)
Absolute Change at Week 4	75 (96.15)
Week 8	75 (96.15)
Absolute Change at Week 8	75 (96.15)
Week 12	74 (94.87)
Absolute Change at Week 12	74 (94.87)
Week 16	75 (96.15)
Absolute Change at Week 16	75 (96.15)
Week 24	78 (100.00)
Absolute Change at Week 24	75 (96.15)
Through Week 24	78 (100.00)
Absolute Change through Week 24	75 (96.15)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	87.39 (15.81)
Week 4 (MMRM)	
n	78
LS mean (SE)	84.62 (1.98)
95% CI of LS mean	(80.67, 88.56)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	-2.78 (1.98)
95% CI of LS mean	(-6.72, 1.16)
Week 8 (MMRM)	
n	78
LS mean (SE)	86.75 (1.83)
95% CI of LS mean	(83.11, 90.39)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	-0.64 (1.83)
95% CI of LS mean	(-4.28, 3.00)
Week 12 (MMRM)	
n	77
LS mean (SE)	92.18 (1.27)
95% CI of LS mean	(89.65, 94.71)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	4.79 (1.27)
95% CI of LS mean	(2.26, 7.32)
Week 16 (MMRM)	
n	78
LS mean (SE)	91.35 (1.53)
95% CI of LS mean	(88.31, 94.39)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	3.96 (1.53)
95% CI of LS mean	(0.92, 7.00)
Week 24	
n	78
Mean (SD)	87.04 (16.08)
Absolute Change at Week 24	
n	78
Mean (SD)	-0.36 (21.01)
Week 24 (MMRM)	
n	78
LS mean (SE)	87.04 (1.81)
95% CI of LS mean	(83.42, 90.65)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	-0.36 (1.81)
95% CI of LS mean	(-3.97, 3.26)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	1.80 (1.31)
95% CI of LS mean	(-0.81, 4.41)
P-value	0.1732

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Respiration

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Health Perception

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: School

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Vitality

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Weight

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	75
Mean (SD)	82.67 (23.48)
Week 4 (MMRM)	
n	75
LS mean (SE)	84.89 (2.18)
95% CI of LS mean	(80.55, 89.23)
Absolute Change at Week 4 (MMRM)	
n	75
LS mean (SE)	2.22 (2.18)
95% CI of LS mean	(-2.12, 6.56)
Week 8 (MMRM)	
n	75
LS mean (SE)	87.56 (2.03)
95% CI of LS mean	(83.51, 91.60)
Absolute Change at Week 8 (MMRM)	
n	75
LS mean (SE)	4.89 (2.03)
95% CI of LS mean	(0.84, 8.94)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	74
LS mean (SE)	88.56 (1.74)
95% CI of LS mean	(85.09, 92.03)
Absolute Change at Week 12 (MMRM)	
n	74
LS mean (SE)	5.89 (1.74)
95% CI of LS mean	(2.42, 9.36)
Week 16 (MMRM)	
n	75
LS mean (SE)	91.26 (1.51)
95% CI of LS mean	(88.25, 94.27)
Absolute Change at Week 16 (MMRM)	
n	75
LS mean (SE)	8.59 (1.51)
95% CI of LS mean	(5.59, 11.60)
Week 24	
n	78
Mean (SD)	88.03 (20.87)
Absolute Change at Week 24	
n	75
Mean (SD)	5.63 (24.19)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 78
Week 24 (MMRM)	
n	78
LS mean (SE)	88.30 (2.21)
95% CI of LS mean	(83.89, 92.71)
Absolute Change at Week 24 (MMRM)	
n	75
LS mean (SE)	5.63 (2.21)
95% CI of LS mean	(1.22, 10.04)
Absolute Change through Week 24 (MMRM)	
n	75
LS mean (SE)	7.11 (1.65)
95% CI of LS mean	(3.81, 10.41)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	74
Mean (SD)	79.73 (21.24)
Week 4 (MMRM)	
n	75
LS mean (SE)	77.48 (3.00)
95% CI of LS mean	(71.49, 83.46)
Absolute Change at Week 4 (MMRM)	
n	74
LS mean (SE)	-2.25 (3.00)
95% CI of LS mean	(-8.24, 3.73)
Week 8 (MMRM)	
n	75
LS mean (SE)	79.73 (2.67)
95% CI of LS mean	(74.40, 85.06)
Absolute Change at Week 8 (MMRM)	
n	74
LS mean (SE)	0.00 (2.67)
95% CI of LS mean	(-5.33, 5.33)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	74
LS mean (SE)	80.07 (2.20)
95% CI of LS mean	(75.68, 84.47)
Absolute Change at Week 12 (MMRM)	
n	73
LS mean (SE)	0.34 (2.20)
95% CI of LS mean	(-4.05, 4.74)
Week 16 (MMRM)	
n	75
LS mean (SE)	83.78 (2.46)
95% CI of LS mean	(78.88, 88.69)
Absolute Change at Week 16 (MMRM)	
n	74
LS mean (SE)	4.05 (2.46)
95% CI of LS mean	(-0.85, 8.96)
Week 24	
n	78
Mean (SD)	84.62 (21.95)
Absolute Change at Week 24	
n	74
Mean (SD)	4.95 (26.28)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 78
Week 24 (MMRM)	
n	78
LS mean (SE)	84.68 (2.50)
95% CI of LS mean	(79.69, 89.68)
Absolute Change at Week 24 (MMRM)	
n	74
LS mean (SE)	4.95 (2.50)
95% CI of LS mean	(-0.04, 9.95)
Absolute Change through Week 24 (MMRM)	
n	74
LS mean (SE)	4.50 (2.05)
95% CI of LS mean	(0.41, 8.59)
P-value	0.0314

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	75
Mean (SD)	81.48 (21.41)
Week 4 (MMRM)	
n	75
LS mean (SE)	81.78 (2.05)
95% CI of LS mean	(77.69, 85.87)
Absolute Change at Week 4 (MMRM)	
n	75
LS mean (SE)	0.30 (2.05)
95% CI of LS mean	(-3.79, 4.39)
Week 8 (MMRM)	
n	75
LS mean (SE)	79.85 (2.23)
95% CI of LS mean	(75.41, 84.29)
Absolute Change at Week 8 (MMRM)	
n	75
LS mean (SE)	-1.63 (2.23)
95% CI of LS mean	(-6.07, 2.81)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	74
LS mean (SE)	83.38 (2.24)
95% CI of LS mean	(78.92, 87.85)
Absolute Change at Week 12 (MMRM)	
n	74
LS mean (SE)	1.90 (2.24)
95% CI of LS mean	(-2.57, 6.37)
Week 16 (MMRM)	
n	75
LS mean (SE)	84.44 (2.17)
95% CI of LS mean	(80.12, 88.77)
Absolute Change at Week 16 (MMRM)	
n	75
LS mean (SE)	2.96 (2.17)
95% CI of LS mean	(-1.37, 7.29)
Week 24	
n	78
Mean (SD)	88.89 (18.17)
Absolute Change at Week 24	
n	75
Mean (SD)	7.26 (17.18)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 78
Week 24 (MMRM)	
n	78
LS mean (SE)	88.74 (1.67)
95% CI of LS mean	(85.42, 92.06)
Absolute Change at Week 24 (MMRM)	
n	75
LS mean (SE)	7.26 (1.67)
95% CI of LS mean	(3.94, 10.58)
Absolute Change through Week 24 (MMRM)	
n	75
LS mean (SE)	5.11 (1.63)
95% CI of LS mean	(1.87, 8.35)
P-value	0.0024

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	75
Mean (SD)	76.50 (14.67)
Week 4 (MMRM)	
n	75
LS mean (SE)	76.52 (1.49)
95% CI of LS mean	(73.54, 79.49)
Absolute Change at Week 4 (MMRM)	
n	75
LS mean (SE)	0.02 (1.49)
95% CI of LS mean	(-2.96, 2.99)
Week 8 (MMRM)	
n	75
LS mean (SE)	77.94 (1.49)
95% CI of LS mean	(74.98, 80.91)
Absolute Change at Week 8 (MMRM)	
n	75
LS mean (SE)	1.44 (1.49)
95% CI of LS mean	(-1.52, 4.41)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	74
LS mean (SE)	79.58 (1.63)
95% CI of LS mean	(76.33, 82.83)
Absolute Change at Week 12 (MMRM)	
n	74
LS mean (SE)	3.08 (1.63)
95% CI of LS mean	(-0.17, 6.33)
Week 16 (MMRM)	
n	75
LS mean (SE)	80.22 (1.66)
95% CI of LS mean	(76.91, 83.53)
Absolute Change at Week 16 (MMRM)	
n	75
LS mean (SE)	3.72 (1.66)
95% CI of LS mean	(0.41, 7.03)
Week 24	
n	78
Mean (SD)	79.81 (15.02)
Absolute Change at Week 24	
n	75
Mean (SD)	3.78 (12.37)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 78
Week 24 (MMRM)	
n	78
LS mean (SE)	80.28 (1.32)
95% CI of LS mean	(77.65, 82.91)
Absolute Change at Week 24 (MMRM)	
n	75
LS mean (SE)	3.78 (1.32)
95% CI of LS mean	(1.15, 6.41)
Absolute Change through Week 24 (MMRM)	
n	75
LS mean (SE)	3.75 (1.34)
95% CI of LS mean	(1.08, 6.42)
P-value	0.0065

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	75
Mean (SD)	87.26 (13.01)
Week 4 (MMRM)	
n	75
LS mean (SE)	86.96 (1.39)
95% CI of LS mean	(84.19, 89.74)
Absolute Change at Week 4 (MMRM)	
n	75
LS mean (SE)	-0.30 (1.39)
95% CI of LS mean	(-3.07, 2.48)
Week 8 (MMRM)	
n	75
LS mean (SE)	85.51 (1.81)
95% CI of LS mean	(81.91, 89.11)
Absolute Change at Week 8 (MMRM)	
n	75
LS mean (SE)	-1.75 (1.81)
95% CI of LS mean	(-5.35, 1.85)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	74
LS mean (SE)	86.31 (1.85)
95% CI of LS mean	(82.63, 89.99)
Absolute Change at Week 12 (MMRM)	
n	74
LS mean (SE)	-0.95 (1.85)
95% CI of LS mean	(-4.63, 2.73)
Week 16 (MMRM)	
n	75
LS mean (SE)	88.52 (1.67)
95% CI of LS mean	(85.19, 91.85)
Absolute Change at Week 16 (MMRM)	
n	75
LS mean (SE)	1.26 (1.67)
95% CI of LS mean	(-2.07, 4.59)
Week 24	
n	78
Mean (SD)	90.38 (14.43)
Absolute Change at Week 24	
n	75
Mean (SD)	3.33 (14.27)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 78
Week 24 (MMRM)	
n	78
LS mean (SE)	90.59 (1.48)
95% CI of LS mean	(87.63, 93.55)
Absolute Change at Week 24 (MMRM)	
n	75
LS mean (SE)	3.33 (1.48)
95% CI of LS mean	(0.37, 6.29)
Absolute Change through Week 24 (MMRM)	
n	75
LS mean (SE)	2.30 (1.32)
95% CI of LS mean	(-0.34, 4.94)
P-value	0.0871

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Social

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	75
Mean (SD)	66.98 (19.25)
Week 4 (MMRM)	
n	75
LS mean (SE)	68.13 (1.60)
95% CI of LS mean	(64.93, 71.32)
Absolute Change at Week 4 (MMRM)	
n	75
LS mean (SE)	1.14 (1.60)
95% CI of LS mean	(-2.05, 4.34)
Week 8 (MMRM)	
n	75
LS mean (SE)	69.02 (1.83)
95% CI of LS mean	(65.37, 72.66)
Absolute Change at Week 8 (MMRM)	
n	75
LS mean (SE)	2.03 (1.83)
95% CI of LS mean	(-1.62, 5.68)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Social

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	74
LS mean (SE)	72.38 (1.70)
95% CI of LS mean	(68.99, 75.77)
Absolute Change at Week 12 (MMRM)	
n	74
LS mean (SE)	5.39 (1.70)
95% CI of LS mean	(2.00, 8.78)
Week 16 (MMRM)	
n	75
LS mean (SE)	72.70 (2.00)
95% CI of LS mean	(68.72, 76.68)
Absolute Change at Week 16 (MMRM)	
n	75
LS mean (SE)	5.71 (2.00)
95% CI of LS mean	(1.73, 9.70)
Week 24	
n	78
Mean (SD)	74.88 (15.34)
Absolute Change at Week 24	
n	75
Mean (SD)	8.67 (19.80)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Social

	VNZ/TEZ/D-IVA N = 78
Week 24 (MMRM)	
n	78
LS mean (SE)	75.65 (1.66)
95% CI of LS mean	(72.34, 78.96)
Absolute Change at Week 24 (MMRM)	
n	75
LS mean (SE)	8.67 (1.66)
95% CI of LS mean	(5.35, 11.98)
Absolute Change through Week 24 (MMRM)	
n	75
LS mean (SE)	7.19 (1.67)
95% CI of LS mean	(3.86, 10.52)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	75
Mean (SD)	76.37 (21.19)
Week 4 (MMRM)	
n	75
LS mean (SE)	79.11 (1.95)
95% CI of LS mean	(75.23, 82.99)
Absolute Change at Week 4 (MMRM)	
n	75
LS mean (SE)	2.74 (1.95)
95% CI of LS mean	(-1.14, 6.62)
Week 8 (MMRM)	
n	75
LS mean (SE)	79.63 (1.85)
95% CI of LS mean	(75.94, 83.32)
Absolute Change at Week 8 (MMRM)	
n	75
LS mean (SE)	3.26 (1.85)
95% CI of LS mean	(-0.44, 6.95)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	74
LS mean (SE)	80.88 (1.92)
95% CI of LS mean	(77.05, 84.70)
Absolute Change at Week 12 (MMRM)	
n	74
LS mean (SE)	4.51 (1.92)
95% CI of LS mean	(0.68, 8.33)
Week 16 (MMRM)	
n	75
LS mean (SE)	79.56 (2.43)
95% CI of LS mean	(74.70, 84.41)
Absolute Change at Week 16 (MMRM)	
n	75
LS mean (SE)	3.19 (2.43)
95% CI of LS mean	(-1.67, 8.04)
Week 24	
n	78
Mean (SD)	81.77 (21.34)
Absolute Change at Week 24	
n	75
Mean (SD)	5.41 (19.82)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 78
Week 24 (MMRM)	
n	78
LS mean (SE)	81.78 (2.07)
95% CI of LS mean	(77.65, 85.91)
Absolute Change at Week 24 (MMRM)	
n	75
LS mean (SE)	5.41 (2.07)
95% CI of LS mean	(1.28, 9.54)
Absolute Change through Week 24 (MMRM)	
n	75
LS mean (SE)	4.30 (1.90)
95% CI of LS mean	(0.52, 8.08)
P-value	0.0265

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	80.13 (26.10)
Week 4 (MMRM)	
n	78
LS mean (SE)	81.34 (1.68)
95% CI of LS mean	(78.00, 84.68)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	1.21 (1.68)
95% CI of LS mean	(-2.13, 4.55)
Week 8 (MMRM)	
n	78
LS mean (SE)	82.48 (1.82)
95% CI of LS mean	(78.85, 86.11)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	2.35 (1.82)
95% CI of LS mean	(-1.28, 5.98)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	84.17 (1.75)
95% CI of LS mean	(80.68, 87.66)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	4.04 (1.75)
95% CI of LS mean	(0.56, 7.53)
Week 16 (MMRM)	
n	78
LS mean (SE)	85.90 (1.85)
95% CI of LS mean	(82.21, 89.59)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	5.77 (1.85)
95% CI of LS mean	(2.08, 9.46)
Week 24	
n	78
Mean (SD)	83.62 (21.39)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	3.49 (17.66)
Week 24 (MMRM)	
n	78
LS mean (SE)	83.62 (1.65)
95% CI of LS mean	(80.32, 86.91)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	3.49 (1.65)
95% CI of LS mean	(0.20, 6.78)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	4.63 (1.55)
95% CI of LS mean	(1.55, 7.71)
P-value	0.0038

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	82.19 (17.39)
Week 4 (MMRM)	
n	78
LS mean (SE)	82.91 (1.73)
95% CI of LS mean	(79.46, 86.35)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	0.71 (1.73)
95% CI of LS mean	(-2.73, 4.16)
Week 8 (MMRM)	
n	78
LS mean (SE)	82.62 (1.62)
95% CI of LS mean	(79.40, 85.85)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	0.43 (1.62)
95% CI of LS mean	(-2.80, 3.65)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	83.98 (1.52)
95% CI of LS mean	(80.94, 87.01)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	1.78 (1.52)
95% CI of LS mean	(-1.25, 4.82)
Week 16 (MMRM)	
n	78
LS mean (SE)	85.47 (1.29)
95% CI of LS mean	(82.91, 88.03)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	3.28 (1.29)
95% CI of LS mean	(0.71, 5.84)
Week 24	
n	78
Mean (SD)	81.48 (16.48)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	-0.71 (16.35)
Week 24 (MMRM)	
n	78
LS mean (SE)	81.48 (1.59)
95% CI of LS mean	(78.32, 84.64)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	-0.71 (1.59)
95% CI of LS mean	(-3.87, 2.45)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	1.28 (1.25)
95% CI of LS mean	(-1.21, 3.77)
P-value	0.3085

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	79.49 (25.61)
Week 4 (MMRM)	
n	78
LS mean (SE)	78.42 (1.87)
95% CI of LS mean	(74.70, 82.14)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	-1.07 (1.87)
95% CI of LS mean	(-4.79, 2.65)
Week 8 (MMRM)	
n	78
LS mean (SE)	79.27 (2.08)
95% CI of LS mean	(75.12, 83.42)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	-0.21 (2.08)
95% CI of LS mean	(-4.36, 3.94)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	78.19 (2.07)
95% CI of LS mean	(74.06, 82.31)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	-1.30 (2.07)
95% CI of LS mean	(-5.42, 2.82)
Week 16 (MMRM)	
n	78
LS mean (SE)	80.98 (1.65)
95% CI of LS mean	(77.70, 84.27)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	1.50 (1.65)
95% CI of LS mean	(-1.79, 4.78)
Week 24	
n	78
Mean (SD)	81.84 (24.05)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	2.35 (18.56)
Week 24 (MMRM)	
n	78
LS mean (SE)	81.84 (1.90)
95% CI of LS mean	(78.05, 85.62)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	2.35 (1.90)
95% CI of LS mean	(-1.43, 6.14)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	1.92 (1.57)
95% CI of LS mean	(-1.19, 5.04)
P-value	0.2230

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	86.52 (12.87)
Week 4 (MMRM)	
n	78
LS mean (SE)	87.01 (1.09)
95% CI of LS mean	(84.85, 89.17)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	0.49 (1.09)
95% CI of LS mean	(-1.67, 2.65)
Week 8 (MMRM)	
n	78
LS mean (SE)	86.71 (1.02)
95% CI of LS mean	(84.67, 88.75)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	0.19 (1.02)
95% CI of LS mean	(-1.84, 2.23)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	89.40 (1.02)
95% CI of LS mean	(87.36, 91.44)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	2.88 (1.02)
95% CI of LS mean	(0.84, 4.92)
Week 16 (MMRM)	
n	78
LS mean (SE)	89.49 (1.07)
95% CI of LS mean	(87.35, 91.62)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	2.97 (1.07)
95% CI of LS mean	(0.84, 5.10)
Week 24	
n	78
Mean (SD)	88.38 (11.03)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	1.86 (12.14)
Week 24 (MMRM)	
n	78
LS mean (SE)	88.38 (1.11)
95% CI of LS mean	(86.17, 90.59)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	1.86 (1.11)
95% CI of LS mean	(-0.35, 4.07)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	2.41 (0.84)
95% CI of LS mean	(0.74, 4.09)
P-value	0.0053

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	86.75 (13.76)
Week 4 (MMRM)	
n	78
LS mean (SE)	82.48 (1.60)
95% CI of LS mean	(79.30, 85.66)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	-4.27 (1.60)
95% CI of LS mean	(-7.46, -1.09)
Week 8 (MMRM)	
n	78
LS mean (SE)	85.90 (1.37)
95% CI of LS mean	(83.17, 88.62)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	-0.85 (1.37)
95% CI of LS mean	(-3.58, 1.87)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	86.87 (1.33)
95% CI of LS mean	(84.22, 89.53)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	0.12 (1.33)
95% CI of LS mean	(-2.53, 2.78)
Week 16 (MMRM)	
n	78
LS mean (SE)	88.46 (1.20)
95% CI of LS mean	(86.07, 90.85)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	1.71 (1.20)
95% CI of LS mean	(-0.68, 4.10)
Week 24	
n	78
Mean (SD)	87.46 (16.64)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	0.71 (16.45)
Week 24 (MMRM)	
n	78
LS mean (SE)	87.46 (1.73)
95% CI of LS mean	(84.02, 90.91)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	0.71 (1.73)
95% CI of LS mean	(-2.73, 4.16)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	1.21 (1.14)
95% CI of LS mean	(-1.07, 3.49)
P-value	0.2934

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	91.88 (13.34)
Week 4 (MMRM)	
n	78
LS mean (SE)	91.03 (1.27)
95% CI of LS mean	(88.49, 93.56)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	-0.85 (1.27)
95% CI of LS mean	(-3.39, 1.68)
Week 8 (MMRM)	
n	78
LS mean (SE)	90.13 (1.26)
95% CI of LS mean	(87.61, 92.64)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	-1.76 (1.26)
95% CI of LS mean	(-4.27, 0.76)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	94.43 (0.85)
95% CI of LS mean	(92.74, 96.12)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	2.55 (0.85)
95% CI of LS mean	(0.86, 4.24)
Week 16 (MMRM)	
n	78
LS mean (SE)	94.18 (1.22)
95% CI of LS mean	(91.74, 96.61)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	2.30 (1.22)
95% CI of LS mean	(-0.14, 4.73)
Week 24	
n	78
Mean (SD)	92.15 (14.76)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	0.27 (11.48)
Week 24 (MMRM)	
n	78
LS mean (SE)	92.15 (1.29)
95% CI of LS mean	(89.57, 94.72)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	0.27 (1.29)
95% CI of LS mean	(-2.31, 2.84)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	1.28 (0.95)
95% CI of LS mean	(-0.61, 3.17)
P-value	0.1805

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	80.45 (17.40)
Week 4 (MMRM)	
n	78
LS mean (SE)	82.48 (1.61)
95% CI of LS mean	(79.28, 85.68)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	2.03 (1.61)
95% CI of LS mean	(-1.17, 5.23)
Week 8 (MMRM)	
n	78
LS mean (SE)	81.41 (1.70)
95% CI of LS mean	(78.03, 84.79)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	0.96 (1.70)
95% CI of LS mean	(-2.42, 4.34)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	84.20 (1.43)
95% CI of LS mean	(81.35, 87.06)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	3.76 (1.43)
95% CI of LS mean	(0.90, 6.61)
Week 16 (MMRM)	
n	78
LS mean (SE)	85.04 (1.58)
95% CI of LS mean	(81.89, 88.20)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	4.59 (1.58)
95% CI of LS mean	(1.44, 7.75)
Week 24	
n	78
Mean (SD)	82.69 (17.03)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	2.24 (15.41)
Week 24 (MMRM)	
n	78
LS mean (SE)	82.69 (1.56)
95% CI of LS mean	(79.59, 85.80)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	2.24 (1.56)
95% CI of LS mean	(-0.86, 5.35)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	3.42 (1.33)
95% CI of LS mean	(0.77, 6.07)
P-value	0.0121

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	69.37 (21.20)
Week 4 (MMRM)	
n	78
LS mean (SE)	76.21 (1.53)
95% CI of LS mean	(73.17, 79.25)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	6.84 (1.53)
95% CI of LS mean	(3.79, 9.88)
Week 8 (MMRM)	
n	78
LS mean (SE)	78.06 (2.16)
95% CI of LS mean	(73.75, 82.38)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	8.69 (2.16)
95% CI of LS mean	(4.37, 13.00)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	75.69 (2.05)
95% CI of LS mean	(71.60, 79.78)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	6.32 (2.05)
95% CI of LS mean	(2.23, 10.41)
Week 16 (MMRM)	
n	78
LS mean (SE)	77.07 (1.63)
95% CI of LS mean	(73.82, 80.31)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	7.69 (1.63)
95% CI of LS mean	(4.45, 10.93)
Week 24	
n	78
Mean (SD)	78.21 (21.07)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	8.83 (19.07)
Week 24 (MMRM)	
n	78
LS mean (SE)	78.21 (1.95)
95% CI of LS mean	(74.32, 82.09)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	8.83 (1.95)
95% CI of LS mean	(4.95, 12.71)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	8.26 (1.58)
95% CI of LS mean	(5.11, 11.41)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	76.67 (12.47)
Week 4 (MMRM)	
n	78
LS mean (SE)	75.21 (1.40)
95% CI of LS mean	(72.43, 78.00)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	-1.45 (1.40)
95% CI of LS mean	(-4.24, 1.33)
Week 8 (MMRM)	
n	78
LS mean (SE)	75.30 (1.11)
95% CI of LS mean	(73.09, 77.51)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	-1.37 (1.11)
95% CI of LS mean	(-3.58, 0.85)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	77.57 (1.22)
95% CI of LS mean	(75.15, 80.00)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	0.91 (1.22)
95% CI of LS mean	(-1.51, 3.33)
Week 16 (MMRM)	
n	78
LS mean (SE)	78.63 (1.25)
95% CI of LS mean	(76.14, 81.12)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	1.97 (1.25)
95% CI of LS mean	(-0.52, 4.46)
Week 24	
n	78
Mean (SD)	75.81 (14.14)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	-0.85 (13.94)
Week 24 (MMRM)	
n	78
LS mean (SE)	75.81 (1.44)
95% CI of LS mean	(72.95, 78.67)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	-0.85 (1.44)
95% CI of LS mean	(-3.71, 2.00)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	0.56 (1.11)
95% CI of LS mean	(-1.65, 2.76)
P-value	0.6167

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	69.23 (35.54)
Week 4 (MMRM)	
n	78
LS mean (SE)	70.51 (2.87)
95% CI of LS mean	(64.79, 76.24)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	1.28 (2.87)
95% CI of LS mean	(-4.44, 7.01)
Week 8 (MMRM)	
n	78
LS mean (SE)	75.21 (2.65)
95% CI of LS mean	(69.94, 80.48)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	5.98 (2.65)
95% CI of LS mean	(0.71, 11.25)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	73.49 (2.70)
95% CI of LS mean	(68.11, 78.87)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	4.26 (2.70)
95% CI of LS mean	(-1.12, 9.64)
Week 16 (MMRM)	
n	78
LS mean (SE)	74.36 (2.68)
95% CI of LS mean	(69.03, 79.69)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	5.13 (2.68)
95% CI of LS mean	(-0.20, 10.46)
Week 24	
n	78
Mean (SD)	74.36 (33.94)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	5.13 (27.95)
Week 24 (MMRM)	
n	78
LS mean (SE)	74.36 (2.85)
95% CI of LS mean	(68.69, 80.03)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	5.13 (2.85)
95% CI of LS mean	(-0.54, 10.80)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	5.13 (2.39)
95% CI of LS mean	(0.37, 9.88)
P-value	0.0348

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.13
Study VX21-121-105: Summary of Pulmonary Exacerbations through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Total number of days (years) of the PEx analysis period	13188 (39.3)
Pulmonary exacerbations	
Number of subjects with events, n (%)	6 (7.69)
Total number of events	6
Observed event rate per year	0.15
Pulmonary exacerbations requiring hospitalization	
Number of subjects with events, n (%)	1 (1.28)
Total number of events	1
Observed event rate per year	0.03
Pulmonary exacerbations requiring IV antibiotic therapy	
Number of subjects with events, n (%)	1 (1.28)
Total number of events	1
Observed event rate per year	0.03
Pulmonary exacerbations requiring hospitalization or IV antibiotic therapy	
Number of subjects with events, n (%)	1 (1.28)
Total number of events	1
Observed event rate per year	0.03

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 3.2.1.14.1
Study VX21-121-105: Time-to-First Pulmonary Exacerbation through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Any Pulmonary Exacerbation	
Overall	
Subjects with Events	6 (7.69)
Subjects Censored	72 (92.31)
Event-free time (weeks)	
75 percent subjects	-
50 percent subjects (Median)	-
25 percent subjects	-

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.1.15.1
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization	
Overall	
Subjects with Events	1 (1.28)
Subjects Censored	77 (98.72)
Event-free time (weeks)	
75 percent subjects	-
50 percent subjects (Median)	-
25 percent subjects	-

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation requiring hospitalization during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.1.16.1
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics	
Overall	
Subjects with Events	1 (1.28)
Subjects Censored	77 (98.72)
Event-free time (weeks)	
75 percent subjects	-
50 percent subjects (Median)	-
25 percent subjects	-

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation requiring IV antibiotics during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.1.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.6683
Region (North America vs. Rest of the World)	0.8154
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.3831

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline $ppFEV_1$ as covariate.
- N/C: model does not converge.

Table 3.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	98.77 (13.79)
Week 24	
n	40
Mean (SD)	99.05 (14.86)
Absolute Change at Week 24	
n	40
Mean (SD)	-0.16 (9.40)
Absolute Change through Week 24 (MMRM)	
n	42
LS mean (SE)	0.03 (1.43)
95% CI of LS mean	(-2.86, 2.92)
P-value	0.9827

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline ppFEV$_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	33
Mean (SD)	100.85 (16.77)
Week 24	
n	30
Mean (SD)	101.19 (11.73)
Absolute Change at Week 24	
n	29
Mean (SD)	-2.61 (6.81)
Absolute Change through Week 24 (MMRM)	
n	32
LS mean (SE)	-0.15 (1.37)
95% CI of LS mean	(-3.00, 2.70)
P-value	0.9123

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline ppFEV$_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	101.64 (12.56)
Week 24	
n	44
Mean (SD)	100.40 (12.97)
Absolute Change at Week 24	
n	44
Mean (SD)	-1.61 (5.72)
Absolute Change through Week 24 (MMRM)	
n	46
LS mean (SE)	-0.65 (0.86)
95% CI of LS mean	(-2.39, 1.10)
P-value	0.4579

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline ppFEV$_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	30
Mean (SD)	96.55 (18.13)
Week 24	
n	26
Mean (SD)	99.24 (14.74)
Absolute Change at Week 24	
n	25
Mean (SD)	-0.44 (11.94)
Absolute Change through Week 24 (MMRM)	
n	28
LS mean (SE)	0.81 (2.14)
95% CI of LS mean	(-3.61, 5.22)
P-value	0.7091

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline ppFEV$_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 24 by Subgroups
Full Analysis Set
LCI$_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	61
Mean (SD)	99.47 (13.81)
Week 24	
n	55
Mean (SD)	99.99 (11.40)
Absolute Change at Week 24	
n	54
Mean (SD)	-1.56 (7.10)
Absolute Change through Week 24 (MMRM)	
n	58
LS mean (SE)	-0.19 (1.00)
95% CI of LS mean	(-2.20, 1.82)
P-value	0.8481

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline ppFEV$_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 24 by Subgroups
Full Analysis Set
LCI$_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	96.30 (23.75)
Week 24	
n	10
Mean (SD)	97.99 (24.49)
Absolute Change at Week 24	
n	10
Mean (SD)	1.68 (14.47)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	1.56 (4.64)
95% CI of LS mean	(-9.05, 12.16)
P-value	0.7451

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline ppFEV$_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.2.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0273
Region (North America vs. Rest of the World)	0.5376
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.3926

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) and subgroup as fixed effect and baseline BMI as covariate.
- N/C: model does not converge.

Table 3.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	17.30 (2.33)
Week 24	
n	44
Mean (SD)	17.41 (2.64)
Absolute Change at Week 24	
n	44
Mean (SD)	0.11 (0.67)
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	0.11 (0.10)
95% CI of LS mean	(-0.08, 0.31)
P-value	0.2538

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	16.23 (1.70)
Week 24	
n	34
Mean (SD)	16.58 (2.07)
Absolute Change at Week 24	
n	34
Mean (SD)	0.35 (0.79)
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	0.35 (0.13)
95% CI of LS mean	(0.08, 0.62)
P-value	0.0137

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	17.39 (2.14)
Week 24	
n	47
Mean (SD)	17.76 (2.41)
Absolute Change at Week 24	
n	47
Mean (SD)	0.37 (0.79)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	0.37 (0.11)
95% CI of LS mean	(0.14, 0.59)
P-value	0.0025

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	15.98 (1.85)
Week 24	
n	31
Mean (SD)	15.97 (2.05)
Absolute Change at Week 24	
n	31
Mean (SD)	-0.01 (0.57)
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	-0.01 (0.10)
95% CI of LS mean	(-0.22, 0.19)
P-value	0.9090

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	16.69 (2.10)
Week 24	
n	62
Mean (SD)	16.88 (2.37)
Absolute Change at Week 24	
n	62
Mean (SD)	0.19 (0.71)
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	0.19 (0.09)
95% CI of LS mean	(0.01, 0.37)
P-value	0.0368

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	17.60 (2.64)
Week 24	
n	10
Mean (SD)	17.94 (2.92)
Absolute Change at Week 24	
n	10
Mean (SD)	0.34 (0.85)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	0.34 (0.23)
95% CI of LS mean	(-0.19, 0.87)
P-value	0.1833

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0135
Region (North America vs. Rest of the World)	0.0510
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.9218

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) and subgroup as fixed effect and baseline BMI z-score as covariate.
- N/C: model does not converge.

Table 3.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	0.30 (0.86)
Week 24	
n	44
Mean (SD)	0.20 (0.97)
Absolute Change at Week 24	
n	44
Mean (SD)	-0.10 (0.26)
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	-0.10 (0.04)
95% CI of LS mean	(-0.18, -0.02)
P-value	0.0138

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	-0.22 (0.81)
Week 24	
n	34
Mean (SD)	-0.21 (0.91)
Absolute Change at Week 24	
n	34
Mean (SD)	0.01 (0.36)
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	0.01 (0.06)
95% CI of LS mean	(-0.11, 0.14)
P-value	0.8290

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	0.28 (0.77)
Week 24	
n	47
Mean (SD)	0.30 (0.81)
Absolute Change at Week 24	
n	47
Mean (SD)	0.02 (0.30)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	0.02 (0.04)
95% CI of LS mean	(-0.07, 0.10)
P-value	0.7044

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	-0.24 (0.94)
Week 24	
n	31
Mean (SD)	-0.39 (1.03)
Absolute Change at Week 24	
n	31
Mean (SD)	-0.15 (0.30)
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	-0.15 (0.05)
95% CI of LS mean	(-0.26, -0.04)
P-value	0.0087

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	-0.01 (0.85)
Week 24	
n	62
Mean (SD)	-0.07 (0.92)
Absolute Change at Week 24	
n	62
Mean (SD)	-0.05 (0.30)
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	-0.05 (0.04)
95% CI of LS mean	(-0.13, 0.02)
P-value	0.1748

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	0.26 (1.01)
Week 24	
n	10
Mean (SD)	0.24 (1.09)
Absolute Change at Week 24	
n	10
Mean (SD)	-0.02 (0.37)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	-0.02 (0.11)
95% CI of LS mean	(-0.26, 0.23)
P-value	0.8646

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.2365
Region (North America vs. Rest of the World)	0.2724
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.5693

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) and subgroup as fixed effect and baseline sweat chloride as covariate.
- N/C: model does not converge.

Table 3.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	43
Mean (SD)	43.05 (22.47)
Week 24	
n	41
Mean (SD)	35.39 (17.60)
Absolute Change at Week 24	
n	41
Mean (SD)	-8.44 (14.34)
Absolute Change through Week 24 (MMRM)	
n	43
LS mean (SE)	-8.86 (1.87)
95% CI of LS mean	(-12.64, -5.08)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for genotype group (F/MF vs rest) and visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	37.07 (18.62)
Week 24	
n	33
Mean (SD)	28.09 (11.40)
Absolute Change at Week 24	
n	33
Mean (SD)	-9.08 (13.67)
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	-8.40 (1.26)
95% CI of LS mean	(-10.96, -5.84)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for genotype group (F/MF vs rest) and visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	39.91 (22.21)
Week 24	
n	45
Mean (SD)	32.22 (15.97)
Absolute Change at Week 24	
n	45
Mean (SD)	-8.11 (15.53)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	-8.06 (1.66)
95% CI of LS mean	(-11.41, -4.70)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for genotype group (F/MF vs rest) and visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	30
Mean (SD)	41.18 (19.12)
Week 24	
n	29
Mean (SD)	32.00 (14.99)
Absolute Change at Week 24	
n	29
Mean (SD)	-9.67 (11.27)
Absolute Change through Week 24 (MMRM)	
n	30
LS mean (SE)	-9.59 (1.56)
95% CI of LS mean	(-12.79, -6.39)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for genotype group (F/MF vs rest) and visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	39.27 (21.31)
Week 24	
n	59
Mean (SD)	32.32 (16.01)
Absolute Change at Week 24	
n	59
Mean (SD)	-7.45 (14.58)
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	-7.77 (1.37)
95% CI of LS mean	(-10.51, -5.02)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for genotype group (F/MF vs rest) and visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	9
Mean (SD)	46.39 (18.60)
Week 24	
n	9
Mean (SD)	32.61 (15.93)
Absolute Change at Week 24	
n	9
Mean (SD)	-13.78 (8.91)
Absolute Change through Week 24 (MMRM)	
n	9
LS mean (SE)	-12.00 (3.19)
95% CI of LS mean	(-25.82, 1.82)
P-value	0.0647

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for genotype group (F/MF vs rest) and visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.4.2.1
Study VX21-121-105: Subgroup Factor Test for
Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0367
Region (North America vs. Rest of the World)	0.7593
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.4396

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Chi-square test.

Table 3.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Non-missing value at Week 24, N1	41
Number of subjects with missing value at Week 24	3
SwCl <60 mmol/L at Week 24, n (%)	36 (81.82)
95% CI for the proportion	(67.29, 91.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 3.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Non-missing value at Week 24, N1	33
Number of subjects with missing value at Week 24	1
SwCl <60 mmol/L at Week 24, n (%)	33 (97.06)
95% CI for the proportion	(84.67, 99.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 3.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Non-missing value at Week 24, N1	45
Number of subjects with missing value at Week 24	2
SwCl <60 mmol/L at Week 24, n (%)	42 (89.36)
95% CI for the proportion	(76.90, 96.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 3.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Non-missing value at Week 24, N1	29
Number of subjects with missing value at Week 24	2
SwCl <60 mmol/L at Week 24, n (%)	27 (87.10)
95% CI for the proportion	(70.17, 96.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 3.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Non-missing value at Week 24, N1	59
Number of subjects with missing value at Week 24	3
SwCl <60 mmol/L at Week 24, n (%)	55 (88.71)
95% CI for the proportion	(78.11, 95.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 3.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Non-missing value at Week 24, N1	9
Number of subjects with missing value at Week 24	1
SwCl <60 mmol/L at Week 24, n (%)	8 (80.00)
95% CI for the proportion	(44.39, 97.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 3.2.2.4.3.1
Study VX21-121-105: Subgroup Factor Test for
Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.1165
Region (North America vs. Rest of the World)	0.6778
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.5571

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Chi-square test.

Table 3.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Non-missing value at Week 24, N1	41
Number of subjects with missing value at Week 24	3
SwCl <30 mmol/L at Week 24, n (%)	18 (40.91)
95% CI for the proportion	(26.34, 56.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 3.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Non-missing value at Week 24, N1	33
Number of subjects with missing value at Week 24	1
SwCl <30 mmol/L at Week 24, n (%)	20 (58.82)
95% CI for the proportion	(40.70, 75.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 3.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Non-missing value at Week 24, N1	45
Number of subjects with missing value at Week 24	2
SwCl <30 mmol/L at Week 24, n (%)	22 (46.81)
95% CI for the proportion	(32.11, 61.92)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 3.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Non-missing value at Week 24, N1	29
Number of subjects with missing value at Week 24	2
SwCl <30 mmol/L at Week 24, n (%)	16 (51.61)
95% CI for the proportion	(33.06, 69.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 3.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Non-missing value at Week 24, N1	59
Number of subjects with missing value at Week 24	3
SwCl <30 mmol/L at Week 24, n (%)	31 (50.00)
95% CI for the proportion	(37.02, 62.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 3.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Non-missing value at Week 24, N1	9
Number of subjects with missing value at Week 24	1
SwCl <30 mmol/L at Week 24, n (%)	4 (40.00)
95% CI for the proportion	(12.16, 73.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 3.2.2.5.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.1330
Region (North America vs. Rest of the World)	0.5313
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.7054

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) and subgroup as fixed effect and baseline weight as covariate.
- N/C: model does not converge.

Table 3.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	30.79 (7.89)
Week 24	
n	44
Mean (SD)	32.26 (8.68)
Absolute Change at Week 24	
n	44
Mean (SD)	1.47 (1.50)
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	1.47 (0.21)
95% CI of LS mean	(1.04, 1.89)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	29.46 (6.96)
Week 24	
n	34
Mean (SD)	31.40 (7.66)
Absolute Change at Week 24	
n	34
Mean (SD)	1.94 (1.52)
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	1.94 (0.26)
95% CI of LS mean	(1.41, 2.47)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	31.70 (7.73)
Week 24	
n	47
Mean (SD)	33.59 (8.43)
Absolute Change at Week 24	
n	47
Mean (SD)	1.89 (1.64)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	1.89 (0.23)
95% CI of LS mean	(1.42, 2.35)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	27.95 (6.57)
Week 24	
n	31
Mean (SD)	29.30 (7.26)
Absolute Change at Week 24	
n	31
Mean (SD)	1.35 (1.26)
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	1.35 (0.22)
95% CI of LS mean	(0.90, 1.80)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	30.01 (7.76)
Week 24	
n	62
Mean (SD)	31.59 (8.48)
Absolute Change at Week 24	
n	62
Mean (SD)	1.58 (1.49)
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	1.58 (0.18)
95% CI of LS mean	(1.22, 1.95)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	33.05 (6.73)
Week 24	
n	10
Mean (SD)	35.22 (7.55)
Absolute Change at Week 24	
n	10
Mean (SD)	2.17 (1.82)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	2.17 (0.62)
95% CI of LS mean	(0.73, 3.62)
P-value	0.0088

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.6.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0153
Region (North America vs. Rest of the World)	0.4962
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.8992

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) and subgroup as fixed effect and baseline weight z-score as covariate.
- N/C: model does not converge.

Table 3.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	0.15 (0.92)
Week 24	
n	44
Mean (SD)	0.09 (1.02)
Absolute Change at Week 24	
n	44
Mean (SD)	-0.06 (0.20)
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	-0.06 (0.03)
95% CI of LS mean	(-0.12, 0.00)
P-value	0.0455

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	-0.18 (0.84)
Week 24	
n	34
Mean (SD)	-0.15 (0.86)
Absolute Change at Week 24	
n	34
Mean (SD)	0.04 (0.24)
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	0.04 (0.04)
95% CI of LS mean	(-0.05, 0.12)
P-value	0.4040

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	0.08 (0.85)
Week 24	
n	47
Mean (SD)	0.10 (0.90)
Absolute Change at Week 24	
n	47
Mean (SD)	0.01 (0.23)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	0.01 (0.03)
95% CI of LS mean	(-0.06, 0.08)
P-value	0.7332

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	-0.12 (0.96)
Week 24	
n	31
Mean (SD)	-0.18 (1.02)
Absolute Change at Week 24	
n	31
Mean (SD)	-0.06 (0.21)
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	-0.06 (0.04)
95% CI of LS mean	(-0.14, 0.01)
P-value	0.1001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	-0.10 (0.90)
Week 24	
n	62
Mean (SD)	-0.13 (0.95)
Absolute Change at Week 24	
n	62
Mean (SD)	-0.03 (0.22)
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	-0.03 (0.03)
95% CI of LS mean	(-0.08, 0.03)
P-value	0.3315

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	0.22 (0.83)
Week 24	
n	10
Mean (SD)	0.24 (0.90)
Absolute Change at Week 24	
n	10
Mean (SD)	0.02 (0.28)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	0.02 (0.08)
95% CI of LS mean	(-0.16, 0.20)
P-value	0.8083

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.7.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0986
Region (North America vs. Rest of the World)	0.4089
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.1315

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) and subgroup as fixed effect and baseline height as covariate.
- N/C: model does not converge.

Table 3.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	132.38 (9.87)
Week 24	
n	44
Mean (SD)	135.00 (9.94)
Absolute Change at Week 24	
n	44
Mean (SD)	2.63 (0.91)
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	2.63 (0.14)
95% CI of LS mean	(2.35, 2.91)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	133.72 (11.39)
Week 24	
n	34
Mean (SD)	136.59 (11.72)
Absolute Change at Week 24	
n	34
Mean (SD)	2.87 (1.20)
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	2.87 (0.20)
95% CI of LS mean	(2.45, 3.28)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	133.98 (10.67)
Week 24	
n	47
Mean (SD)	136.47 (10.82)
Absolute Change at Week 24	
n	47
Mean (SD)	2.49 (0.99)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	2.49 (0.14)
95% CI of LS mean	(2.20, 2.78)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	131.42 (10.23)
Week 24	
n	31
Mean (SD)	134.52 (10.60)
Absolute Change at Week 24	
n	31
Mean (SD)	3.10 (1.03)
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	3.10 (0.19)
95% CI of LS mean	(2.71, 3.49)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	132.93 (10.44)
Week 24	
n	62
Mean (SD)	135.58 (10.56)
Absolute Change at Week 24	
n	62
Mean (SD)	2.65 (1.08)
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	2.65 (0.14)
95% CI of LS mean	(2.37, 2.92)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	136.69 (11.47)
Week 24	
n	10
Mean (SD)	139.76 (11.86)
Absolute Change at Week 24	
n	10
Mean (SD)	3.07 (0.70)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	3.07 (0.47)
95% CI of LS mean	(1.89, 4.25)
P-value	0.0009

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.8.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.1914
Region (North America vs. Rest of the World)	0.5643
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.2901

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) and subgroup as fixed effect and baseline height z-score as covariate.
- N/C: model does not converge.

Table 3.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	-0.09 (0.97)
Week 24	
n	44
Mean (SD)	-0.08 (0.97)
Absolute Change at Week 24	
n	44
Mean (SD)	0.02 (0.16)
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	0.02 (0.02)
95% CI of LS mean	(-0.03, 0.07)
P-value	0.5165

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	0.06 (0.91)
Week 24	
n	34
Mean (SD)	0.06 (0.97)
Absolute Change at Week 24	
n	34
Mean (SD)	0.01 (0.19)
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	0.01 (0.03)
95% CI of LS mean	(-0.06, 0.07)
P-value	0.8353

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	-0.12 (0.98)
Week 24	
n	47
Mean (SD)	-0.14 (1.00)
Absolute Change at Week 24	
n	47
Mean (SD)	-0.01 (0.18)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	-0.01 (0.03)
95% CI of LS mean	(-0.06, 0.04)
P-value	0.6255

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	0.12 (0.88)
Week 24	
n	31
Mean (SD)	0.17 (0.89)
Absolute Change at Week 24	
n	31
Mean (SD)	0.05 (0.16)
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	0.05 (0.03)
95% CI of LS mean	(-0.01, 0.11)
P-value	0.0984

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	-0.10 (0.97)
Week 24	
n	62
Mean (SD)	-0.10 (0.97)
Absolute Change at Week 24	
n	62
Mean (SD)	0.00 (0.18)
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	0.00 (0.02)
95% CI of LS mean	(-0.04, 0.05)
P-value	0.9010

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	0.10 (0.82)
Week 24	
n	10
Mean (SD)	0.15 (0.86)
Absolute Change at Week 24	
n	10
Mean (SD)	0.06 (0.13)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	0.06 (0.05)
95% CI of LS mean	(-0.06, 0.17)
P-value	0.2747

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.9.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0004
Region (North America vs. Rest of the World)	0.5202
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.8616

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline $LCI_{2.5}$ as covariate.
- N/C: model does not converge.

Table 3.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	40
Mean (SD)	6.60 (0.78)
Week 24	
n	34
Mean (SD)	6.35 (0.43)
Absolute Change at Week 24	
n	32
Mean (SD)	-0.28 (0.53)
Absolute Change through Week 24 (MMRM)	
n	32
LS mean (SE)	-0.20 (0.05)
95% CI of LS mean	(-0.31, -0.09)
P-value	0.0013

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 3.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	32
Mean (SD)	6.67 (0.71)
Week 24	
n	27
Mean (SD)	6.60 (0.64)
Absolute Change at Week 24	
n	26
Mean (SD)	-0.03 (0.53)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	0.05 (0.07)
95% CI of LS mean	(-0.10, 0.20)
P-value	0.5087

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 3.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	43
Mean (SD)	6.60 (0.68)
Week 24	
n	37
Mean (SD)	6.47 (0.56)
Absolute Change at Week 24	
n	35
Mean (SD)	-0.15 (0.54)
Absolute Change through Week 24 (MMRM)	
n	35
LS mean (SE)	-0.10 (0.06)
95% CI of LS mean	(-0.22, 0.03)
P-value	0.1210

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 3.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	29
Mean (SD)	6.67 (0.84)
Week 24	
n	24
Mean (SD)	6.45 (0.53)
Absolute Change at Week 24	
n	23
Mean (SD)	-0.19 (0.56)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	-0.07 (0.09)
95% CI of LS mean	(-0.24, 0.11)
P-value	0.4571

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 3.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	6.40 (0.46)
Week 24	
n	50
Mean (SD)	6.34 (0.47)
Absolute Change at Week 24	
n	50
Mean (SD)	-0.06 (0.48)
Absolute Change through Week 24 (MMRM)	
n	50
LS mean (SE)	-0.01 (0.05)
95% CI of LS mean	(-0.11, 0.08)
P-value	0.7508

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 3.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	8.04 (0.60)
Week 24	
n	8
Mean (SD)	6.97 (0.52)
Absolute Change at Week 24	
n	8
Mean (SD)	-0.82 (0.47)
Absolute Change through Week 24 (MMRM)	
n	8
LS mean (SE)	-0.47 (0.18)
95% CI of LS mean	(-0.91, -0.02)
P-value	0.0421

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.3066
Region (North America vs. Rest of the World)	0.2465
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.8058

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Respiratory domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	42
Mean (SD)	84.33 (14.04)
Week 4 (MMRM)	
n	42
LS mean (SE)	85.12 (1.62)
95% CI of LS mean	(81.84, 88.40)
Absolute Change at Week 4 (MMRM)	
n	42
LS mean (SE)	0.79 (1.62)
95% CI of LS mean	(-2.49, 4.08)
Week 8 (MMRM)	
n	42
LS mean (SE)	85.12 (2.14)
95% CI of LS mean	(80.80, 89.44)
Absolute Change at Week 8 (MMRM)	
n	42
LS mean (SE)	0.79 (2.14)
95% CI of LS mean	(-3.53, 5.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 12 (MMRM)	
n	41
LS mean (SE)	88.33 (1.69)
95% CI of LS mean	(84.91, 91.76)
Absolute Change at Week 12 (MMRM)	
n	41
LS mean (SE)	4.01 (1.69)
95% CI of LS mean	(0.59, 7.43)
Week 16 (MMRM)	
n	42
LS mean (SE)	90.28 (1.70)
95% CI of LS mean	(86.84, 93.72)
Absolute Change at Week 16 (MMRM)	
n	42
LS mean (SE)	5.95 (1.70)
95% CI of LS mean	(2.51, 9.39)
Week 24	
n	44
Mean (SD)	86.55 (15.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 24	
n	42
Mean (SD)	2.58 (16.72)
Week 24 (MMRM)	
n	44
LS mean (SE)	86.90 (2.24)
95% CI of LS mean	(82.38, 91.43)
Absolute Change at Week 24 (MMRM)	
n	42
LS mean (SE)	2.58 (2.24)
95% CI of LS mean	(-1.95, 7.11)
Absolute Change through Week 24 (MMRM)	
n	42
LS mean (SE)	4.27 (1.53)
95% CI of LS mean	(1.17, 7.37)
P-value	0.0082

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	33
Mean (SD)	85.35 (18.64)
Week 4 (MMRM)	
n	33
LS mean (SE)	85.86 (3.00)
95% CI of LS mean	(79.74, 91.97)
Absolute Change at Week 4 (MMRM)	
n	33
LS mean (SE)	0.51 (3.00)
95% CI of LS mean	(-5.61, 6.62)
Week 8 (MMRM)	
n	33
LS mean (SE)	88.13 (2.92)
95% CI of LS mean	(82.17, 94.09)
Absolute Change at Week 8 (MMRM)	
n	33
LS mean (SE)	2.78 (2.92)
95% CI of LS mean	(-3.18, 8.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 12 (MMRM)	
n	33
LS mean (SE)	92.93 (1.75)
95% CI of LS mean	(89.36, 96.50)
Absolute Change at Week 12 (MMRM)	
n	33
LS mean (SE)	7.58 (1.75)
95% CI of LS mean	(4.01, 11.14)
Week 16 (MMRM)	
n	33
LS mean (SE)	91.67 (1.96)
95% CI of LS mean	(87.67, 95.66)
Absolute Change at Week 16 (MMRM)	
n	33
LS mean (SE)	6.31 (1.96)
95% CI of LS mean	(2.32, 10.31)
Week 24	
n	34
Mean (SD)	84.80 (16.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 24	
n	33
Mean (SD)	0.76 (21.18)
Week 24 (MMRM)	
n	34
LS mean (SE)	86.11 (2.56)
95% CI of LS mean	(80.90, 91.33)
Absolute Change at Week 24 (MMRM)	
n	33
LS mean (SE)	0.76 (2.56)
95% CI of LS mean	(-4.46, 5.97)
Absolute Change through Week 24 (MMRM)	
n	33
LS mean (SE)	3.54 (1.91)
95% CI of LS mean	(-0.36, 7.44)
P-value	0.0740

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	82.80 (17.32)
Week 4 (MMRM)	
n	47
LS mean (SE)	82.09 (2.36)
95% CI of LS mean	(77.34, 86.85)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	-0.71 (2.36)
95% CI of LS mean	(-5.46, 4.05)
Week 8 (MMRM)	
n	47
LS mean (SE)	85.11 (2.28)
95% CI of LS mean	(80.51, 89.70)
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	2.30 (2.28)
95% CI of LS mean	(-2.29, 6.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 12 (MMRM)	
n	47
LS mean (SE)	89.54 (1.66)
95% CI of LS mean	(86.20, 92.88)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	6.74 (1.66)
95% CI of LS mean	(3.40, 10.07)
Week 16 (MMRM)	
n	47
LS mean (SE)	89.89 (1.73)
95% CI of LS mean	(86.41, 93.37)
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	7.09 (1.73)
95% CI of LS mean	(3.61, 10.57)
Week 24	
n	47
Mean (SD)	85.11 (15.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 24	
n	47
Mean (SD)	2.30 (19.48)
Week 24 (MMRM)	
n	47
LS mean (SE)	85.11 (2.14)
95% CI of LS mean	(80.80, 89.41)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	2.30 (2.14)
95% CI of LS mean	(-2.00, 6.61)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	4.70 (1.59)
95% CI of LS mean	(1.51, 7.89)
P-value	0.0048

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	28
Mean (SD)	88.10 (13.50)
Week 4 (MMRM)	
n	28
LS mean (SE)	91.07 (1.94)
95% CI of LS mean	(87.08, 95.07)
Absolute Change at Week 4 (MMRM)	
n	28
LS mean (SE)	2.98 (1.94)
95% CI of LS mean	(-1.02, 6.97)
Week 8 (MMRM)	
n	28
LS mean (SE)	88.69 (2.45)
95% CI of LS mean	(83.64, 93.74)
Absolute Change at Week 8 (MMRM)	
n	28
LS mean (SE)	0.60 (2.45)
95% CI of LS mean	(-4.45, 5.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 12 (MMRM)	
n	27
LS mean (SE)	92.06 (2.26)
95% CI of LS mean	(87.41, 96.72)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	3.97 (2.26)
95% CI of LS mean	(-0.69, 8.63)
Week 16 (MMRM)	
n	28
LS mean (SE)	92.56 (2.35)
95% CI of LS mean	(87.70, 97.42)
Absolute Change at Week 16 (MMRM)	
n	28
LS mean (SE)	4.46 (2.35)
95% CI of LS mean	(-0.39, 9.32)
Week 24	
n	31
Mean (SD)	86.83 (16.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 24	
n	28
Mean (SD)	0.89 (17.62)
Week 24 (MMRM)	
n	31
LS mean (SE)	88.99 (2.64)
95% CI of LS mean	(83.55, 94.43)
Absolute Change at Week 24 (MMRM)	
n	28
LS mean (SE)	0.89 (2.64)
95% CI of LS mean	(-4.54, 6.33)
Absolute Change through Week 24 (MMRM)	
n	28
LS mean (SE)	2.68 (2.01)
95% CI of LS mean	(-1.48, 6.84)
P-value	0.1957

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	59
Mean (SD)	84.18 (16.50)
Week 4 (MMRM)	
n	59
LS mean (SE)	85.88 (1.74)
95% CI of LS mean	(82.40, 89.35)
Absolute Change at Week 4 (MMRM)	
n	59
LS mean (SE)	1.69 (1.74)
95% CI of LS mean	(-1.78, 5.17)
Week 8 (MMRM)	
n	59
LS mean (SE)	87.43 (2.01)
95% CI of LS mean	(83.40, 91.45)
Absolute Change at Week 8 (MMRM)	
n	59
LS mean (SE)	3.25 (2.01)
95% CI of LS mean	(-0.78, 7.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 12 (MMRM)	
n	58
LS mean (SE)	90.77 (1.57)
95% CI of LS mean	(87.62, 93.91)
Absolute Change at Week 12 (MMRM)	
n	58
LS mean (SE)	6.59 (1.57)
95% CI of LS mean	(3.44, 9.73)
Week 16 (MMRM)	
n	59
LS mean (SE)	91.38 (1.50)
95% CI of LS mean	(88.39, 94.38)
Absolute Change at Week 16 (MMRM)	
n	59
LS mean (SE)	7.20 (1.50)
95% CI of LS mean	(4.21, 10.20)
Week 24	
n	62
Mean (SD)	84.54 (16.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 24	
n	59
Mean (SD)	1.27 (19.50)
Week 24 (MMRM)	
n	62
LS mean (SE)	85.45 (1.98)
95% CI of LS mean	(81.49, 89.41)
Absolute Change at Week 24 (MMRM)	
n	59
LS mean (SE)	1.27 (1.98)
95% CI of LS mean	(-2.69, 5.23)
Absolute Change through Week 24 (MMRM)	
n	59
LS mean (SE)	4.24 (1.39)
95% CI of LS mean	(1.45, 7.02)
P-value	0.0035

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	90.00 (15.61)
Week 4 (MMRM)	
n	10
LS mean (SE)	85.00 (6.12)
95% CI of LS mean	(70.88, 99.12)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	-5.00 (6.12)
95% CI of LS mean	(-19.12, 9.12)
Week 8 (MMRM)	
n	10
LS mean (SE)	85.83 (2.87)
95% CI of LS mean	(49.32, 122.34)
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	-4.17 (2.87)
95% CI of LS mean	(-40.68, 32.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 12 (MMRM)	
n	10
LS mean (SE)	89.17 (4.73)
95% CI of LS mean	(66.22, 112.12)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	-0.83 (4.73)
95% CI of LS mean	(-23.78, 22.12)
Week 16 (MMRM)	
n	10
LS mean (SE)	92.50 (5.24)
95% CI of LS mean	(76.27, 108.73)
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	2.50 (5.24)
95% CI of LS mean	(-13.73, 18.73)
Week 24	
n	10
Mean (SD)	95.00 (8.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 24	
n	10
Mean (SD)	5.00 (20.11)
Week 24 (MMRM)	
n	10
LS mean (SE)	95.00 (6.52)
95% CI of LS mean	(75.72, 114.28)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	5.00 (6.52)
95% CI of LS mean	(-14.28, 24.28)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	3.75 (5.61)
95% CI of LS mean	(-14.40, 21.90)
P-value	0.5529

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.3142
Region (North America vs. Rest of the World)	0.2057
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.6296

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Respiratory domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	86.84 (14.27)
Week 4 (MMRM)	
n	44
LS mean (SE)	82.95 (2.47)
95% CI of LS mean	(77.98, 87.93)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	-3.89 (2.47)
95% CI of LS mean	(-8.87, 1.09)
Week 8 (MMRM)	
n	44
LS mean (SE)	84.22 (2.53)
95% CI of LS mean	(79.10, 89.33)
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	-2.63 (2.53)
95% CI of LS mean	(-7.74, 2.49)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 12 (MMRM)	
n	43
LS mean (SE)	91.91 (1.29)
95% CI of LS mean	(89.31, 94.50)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	5.06 (1.29)
95% CI of LS mean	(2.46, 7.66)
Week 16 (MMRM)	
n	44
LS mean (SE)	88.96 (2.27)
95% CI of LS mean	(84.39, 93.54)
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	2.12 (2.27)
95% CI of LS mean	(-2.46, 6.70)
Week 24	
n	44
Mean (SD)	88.38 (15.24)
Absolute Change at Week 24	
n	44
Mean (SD)	1.54 (17.88)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 24 (MMRM)	
n	44
LS mean (SE)	88.38 (2.23)
95% CI of LS mean	(83.88, 92.88)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	1.54 (2.23)
95% CI of LS mean	(-2.96, 6.04)
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	1.83 (1.73)
95% CI of LS mean	(-1.66, 5.32)
P-value	0.2957

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	88.10 (17.81)
Week 4 (MMRM)	
n	34
LS mean (SE)	86.76 (3.20)
95% CI of LS mean	(80.26, 93.27)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	-1.34 (3.20)
95% CI of LS mean	(-7.84, 5.16)
Week 8 (MMRM)	
n	34
LS mean (SE)	90.03 (2.44)
95% CI of LS mean	(85.07, 95.00)
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	1.93 (2.44)
95% CI of LS mean	(-3.04, 6.89)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 12 (MMRM)	
n	34
LS mean (SE)	92.48 (2.32)
95% CI of LS mean	(87.75, 97.21)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	4.38 (2.32)
95% CI of LS mean	(-0.35, 9.11)
Week 16 (MMRM)	
n	34
LS mean (SE)	94.44 (1.80)
95% CI of LS mean	(90.78, 98.11)
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	6.34 (1.80)
95% CI of LS mean	(2.68, 10.00)
Week 24	
n	34
Mean (SD)	85.29 (17.19)
Absolute Change at Week 24	
n	34
Mean (SD)	-2.81 (24.53)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 24 (MMRM)	
n	34
LS mean (SE)	85.29 (2.99)
95% CI of LS mean	(79.20, 91.39)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	-2.81 (2.99)
95% CI of LS mean	(-8.91, 3.29)
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	1.76 (2.01)
95% CI of LS mean	(-2.34, 5.87)
P-value	0.3872

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	85.84 (17.50)
Week 4 (MMRM)	
n	47
LS mean (SE)	84.04 (2.31)
95% CI of LS mean	(79.40, 88.68)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	-1.80 (2.31)
95% CI of LS mean	(-6.44, 2.84)
Week 8 (MMRM)	
n	47
LS mean (SE)	86.88 (2.30)
95% CI of LS mean	(82.26, 91.50)
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	1.04 (2.30)
95% CI of LS mean	(-3.58, 5.66)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 12 (MMRM)	
n	47
LS mean (SE)	93.03 (1.68)
95% CI of LS mean	(89.65, 96.40)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	7.19 (1.68)
95% CI of LS mean	(3.81, 10.56)
Week 16 (MMRM)	
n	47
LS mean (SE)	92.55 (1.38)
95% CI of LS mean	(89.77, 95.34)
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	6.71 (1.38)
95% CI of LS mean	(3.93, 9.50)
Week 24	
n	47
Mean (SD)	87.59 (15.59)
Absolute Change at Week 24	
n	47
Mean (SD)	1.75 (19.92)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 24 (MMRM)	
n	47
LS mean (SE)	87.59 (2.23)
95% CI of LS mean	(83.10, 92.08)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	1.75 (2.23)
95% CI of LS mean	(-2.74, 6.24)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	4.23 (1.38)
95% CI of LS mean	(1.45, 7.01)
P-value	0.0037

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	89.75 (12.75)
Week 4 (MMRM)	
n	31
LS mean (SE)	85.48 (3.61)
95% CI of LS mean	(78.10, 92.86)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	-4.27 (3.61)
95% CI of LS mean	(-11.65, 3.12)
Week 8 (MMRM)	
n	31
LS mean (SE)	86.56 (3.01)
95% CI of LS mean	(80.35, 92.77)
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	-3.19 (3.01)
95% CI of LS mean	(-9.40, 3.02)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 12 (MMRM)	
n	30
LS mean (SE)	90.87 (1.90)
95% CI of LS mean	(86.98, 94.76)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	1.12 (1.90)
95% CI of LS mean	(-2.77, 5.01)
Week 16 (MMRM)	
n	31
LS mean (SE)	89.53 (3.06)
95% CI of LS mean	(83.28, 95.79)
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	-0.22 (3.06)
95% CI of LS mean	(-6.47, 6.04)
Week 24	
n	31
Mean (SD)	86.20 (17.03)
Absolute Change at Week 24	
n	31
Mean (SD)	-3.55 (22.50)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 24 (MMRM)	
n	31
LS mean (SE)	86.20 (3.25)
95% CI of LS mean	(79.53, 92.87)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	-3.55 (3.25)
95% CI of LS mean	(-10.22, 3.12)
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	-1.88 (2.54)
95% CI of LS mean	(-7.09, 3.32)
P-value	0.4655

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	86.83 (16.08)
Week 4 (MMRM)	
n	62
LS mean (SE)	83.33 (2.40)
95% CI of LS mean	(78.53, 88.14)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	-3.49 (2.40)
95% CI of LS mean	(-8.30, 1.31)
Week 8 (MMRM)	
n	62
LS mean (SE)	86.83 (2.14)
95% CI of LS mean	(82.54, 91.12)
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	0.00 (2.14)
95% CI of LS mean	(-4.29, 4.29)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 12 (MMRM)	
n	61
LS mean (SE)	92.42 (1.45)
95% CI of LS mean	(89.51, 95.32)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	5.59 (1.45)
95% CI of LS mean	(2.69, 8.50)
Week 16 (MMRM)	
n	62
LS mean (SE)	90.82 (1.83)
95% CI of LS mean	(87.17, 94.48)
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	4.00 (1.83)
95% CI of LS mean	(0.34, 7.65)
Week 24	
n	62
Mean (SD)	85.13 (17.27)
Absolute Change at Week 24	
n	62
Mean (SD)	-1.70 (21.82)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 24 (MMRM)	
n	62
LS mean (SE)	85.13 (2.18)
95% CI of LS mean	(80.76, 89.49)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	-1.70 (2.18)
95% CI of LS mean	(-6.07, 2.66)
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	1.15 (1.58)
95% CI of LS mean	(-2.02, 4.31)
P-value	0.4718

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	87.22 (17.18)
Week 4 (MMRM)	
n	10
LS mean (SE)	91.67 (2.90)
95% CI of LS mean	(84.49, 98.84)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	4.44 (2.90)
95% CI of LS mean	(-2.73, 11.62)
Week 8 (MMRM)	
n	10
LS mean (SE)	86.11 (2.60)
95% CI of LS mean	(79.74, 92.49)
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	-1.11 (2.60)
95% CI of LS mean	(-7.49, 5.26)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 12 (MMRM)	
n	10
LS mean (SE)	89.44 (3.22)
95% CI of LS mean	(82.09, 96.79)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	2.22 (3.22)
95% CI of LS mean	(-5.13, 9.57)
Week 16 (MMRM)	
n	10
LS mean (SE)	93.89 (2.11)
95% CI of LS mean	(87.92, 99.86)
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	6.67 (2.11)
95% CI of LS mean	(0.70, 12.64)
Week 24	
n	10
Mean (SD)	96.11 (5.27)
Absolute Change at Week 24	
n	10
Mean (SD)	8.89 (17.99)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 24 (MMRM)	
n	10
LS mean (SE)	96.11 (4.40)
95% CI of LS mean	(84.88, 107.35)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	8.89 (4.40)
95% CI of LS mean	(-2.35, 20.12)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	7.78 (3.02)
95% CI of LS mean	(-0.93, 16.49)
P-value	0.0674

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set
Domain: Body

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.8997
Region (North America vs. Rest of the World)	0.3891
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.8784

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Body domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set
Domain: Digestion

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.5173
Region (North America vs. Rest of the World)	0.1967
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.4427

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Digestion domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set
Domain: Eat

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.2115
Region (North America vs. Rest of the World)	0.2904
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.9535

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Eat domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set
Domain: Emotion

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.2229
Region (North America vs. Rest of the World)	0.5092
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.3430

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Emotion domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set
Domain: Physical

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.3477
Region (North America vs. Rest of the World)	0.6533
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.9955

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Physical domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set
Domain: Social

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.6920
Region (North America vs. Rest of the World)	0.3202
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.9277

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Social domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set
Domain: Treatment Burden

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.9678
Region (North America vs. Rest of the World)	0.0379
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.4272

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Treatment Burden domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	42
Mean (SD)	85.71 (21.43)
Week 4 (MMRM)	
n	42
LS mean (SE)	86.77 (3.19)
95% CI of LS mean	(80.33, 93.22)
Absolute Change at Week 4 (MMRM)	
n	42
LS mean (SE)	1.06 (3.19)
95% CI of LS mean	(-5.38, 7.50)
Week 8 (MMRM)	
n	42
LS mean (SE)	89.95 (2.59)
95% CI of LS mean	(84.71, 95.19)
Absolute Change at Week 8 (MMRM)	
n	42
LS mean (SE)	4.23 (2.59)
95% CI of LS mean	(-1.01, 9.47)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 12 (MMRM)	
n	41
LS mean (SE)	88.78 (2.23)
95% CI of LS mean	(84.28, 93.29)
Absolute Change at Week 12 (MMRM)	
n	41
LS mean (SE)	3.07 (2.23)
95% CI of LS mean	(-1.43, 7.57)
Week 16 (MMRM)	
n	42
LS mean (SE)	92.06 (1.86)
95% CI of LS mean	(88.30, 95.83)
Absolute Change at Week 16 (MMRM)	
n	42
LS mean (SE)	6.35 (1.86)
95% CI of LS mean	(2.58, 10.11)
Week 24	
n	44
Mean (SD)	89.39 (19.90)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 24	
n	42
Mean (SD)	4.23 (25.14)
Week 24 (MMRM)	
n	44
LS mean (SE)	89.95 (2.94)
95% CI of LS mean	(84.00, 95.90)
Absolute Change at Week 24 (MMRM)	
n	42
LS mean (SE)	4.23 (2.94)
95% CI of LS mean	(-1.72, 10.18)
Absolute Change through Week 24 (MMRM)	
n	42
LS mean (SE)	5.29 (2.08)
95% CI of LS mean	(1.08, 9.50)
P-value	0.0151

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	33
Mean (SD)	78.79 (25.66)
Week 4 (MMRM)	
n	33
LS mean (SE)	82.49 (2.64)
95% CI of LS mean	(77.08, 87.90)
Absolute Change at Week 4 (MMRM)	
n	33
LS mean (SE)	3.70 (2.64)
95% CI of LS mean	(-1.71, 9.11)
Week 8 (MMRM)	
n	33
LS mean (SE)	84.51 (3.41)
95% CI of LS mean	(77.56, 91.46)
Absolute Change at Week 8 (MMRM)	
n	33
LS mean (SE)	5.72 (3.41)
95% CI of LS mean	(-1.23, 12.68)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 12 (MMRM)	
n	33
LS mean (SE)	88.22 (2.89)
95% CI of LS mean	(82.31, 94.12)
Absolute Change at Week 12 (MMRM)	
n	33
LS mean (SE)	9.43 (2.89)
95% CI of LS mean	(3.53, 15.33)
Week 16 (MMRM)	
n	33
LS mean (SE)	90.24 (2.41)
95% CI of LS mean	(85.32, 95.15)
Absolute Change at Week 16 (MMRM)	
n	33
LS mean (SE)	11.45 (2.41)
95% CI of LS mean	(6.53, 16.36)
Week 24	
n	34
Mean (SD)	86.27 (22.23)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 24	
n	33
Mean (SD)	7.41 (23.19)
Week 24 (MMRM)	
n	34
LS mean (SE)	86.20 (3.29)
95% CI of LS mean	(79.49, 92.90)
Absolute Change at Week 24 (MMRM)	
n	33
LS mean (SE)	7.41 (3.29)
95% CI of LS mean	(0.70, 14.11)
Absolute Change through Week 24 (MMRM)	
n	33
LS mean (SE)	9.43 (2.58)
95% CI of LS mean	(4.16, 14.70)
P-value	0.0010

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	78.49 (25.10)
Week 4 (MMRM)	
n	47
LS mean (SE)	83.22 (3.15)
95% CI of LS mean	(76.87, 89.56)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	4.73 (3.15)
95% CI of LS mean	(-1.62, 11.08)
Week 8 (MMRM)	
n	47
LS mean (SE)	85.34 (2.84)
95% CI of LS mean	(79.61, 91.07)
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	6.86 (2.84)
95% CI of LS mean	(1.12, 12.59)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 12 (MMRM)	
n	47
LS mean (SE)	89.13 (1.99)
95% CI of LS mean	(85.12, 93.13)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	10.64 (1.99)
95% CI of LS mean	(6.63, 14.65)
Week 16 (MMRM)	
n	47
LS mean (SE)	90.07 (2.18)
95% CI of LS mean	(85.67, 94.47)
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	11.58 (2.18)
95% CI of LS mean	(7.19, 15.98)
Week 24	
n	47
Mean (SD)	85.11 (24.33)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 24	
n	47
Mean (SD)	6.62 (28.34)
Week 24 (MMRM)	
n	47
LS mean (SE)	85.11 (3.37)
95% CI of LS mean	(78.32, 91.89)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	6.62 (3.37)
95% CI of LS mean	(-0.17, 13.41)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	9.10 (2.51)
95% CI of LS mean	(4.05, 14.16)
P-value	0.0007

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	28
Mean (SD)	89.68 (18.87)
Week 4 (MMRM)	
n	28
LS mean (SE)	87.70 (2.54)
95% CI of LS mean	(82.47, 92.93)
Absolute Change at Week 4 (MMRM)	
n	28
LS mean (SE)	-1.98 (2.54)
95% CI of LS mean	(-7.22, 3.25)
Week 8 (MMRM)	
n	28
LS mean (SE)	91.27 (2.62)
95% CI of LS mean	(85.88, 96.66)
Absolute Change at Week 8 (MMRM)	
n	28
LS mean (SE)	1.59 (2.62)
95% CI of LS mean	(-3.80, 6.98)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 12 (MMRM)	
n	27
LS mean (SE)	87.62 (3.23)
95% CI of LS mean	(80.98, 94.25)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	-2.07 (3.23)
95% CI of LS mean	(-8.70, 4.57)
Week 16 (MMRM)	
n	28
LS mean (SE)	93.25 (1.85)
95% CI of LS mean	(89.43, 97.08)
Absolute Change at Week 16 (MMRM)	
n	28
LS mean (SE)	3.57 (1.85)
95% CI of LS mean	(-0.26, 7.40)
Week 24	
n	31
Mean (SD)	92.47 (13.27)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 24	
n	28
Mean (SD)	3.97 (15.18)
Week 24 (MMRM)	
n	31
LS mean (SE)	93.65 (1.86)
95% CI of LS mean	(89.82, 97.48)
Absolute Change at Week 24 (MMRM)	
n	28
LS mean (SE)	3.97 (1.86)
95% CI of LS mean	(0.14, 7.80)
Absolute Change through Week 24 (MMRM)	
n	28
LS mean (SE)	3.77 (1.56)
95% CI of LS mean	(0.55, 6.99)
P-value	0.0238

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	59
Mean (SD)	83.80 (23.64)
Week 4 (MMRM)	
n	59
LS mean (SE)	84.56 (2.49)
95% CI of LS mean	(79.56, 89.55)
Absolute Change at Week 4 (MMRM)	
n	59
LS mean (SE)	0.75 (2.49)
95% CI of LS mean	(-4.24, 5.75)
Week 8 (MMRM)	
n	59
LS mean (SE)	90.02 (1.95)
95% CI of LS mean	(86.12, 93.92)
Absolute Change at Week 8 (MMRM)	
n	59
LS mean (SE)	6.21 (1.95)
95% CI of LS mean	(2.31, 10.12)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 12 (MMRM)	
n	58
LS mean (SE)	88.83 (1.98)
95% CI of LS mean	(84.87, 92.80)
Absolute Change at Week 12 (MMRM)	
n	58
LS mean (SE)	5.03 (1.98)
95% CI of LS mean	(1.06, 9.00)
Week 16 (MMRM)	
n	59
LS mean (SE)	91.71 (1.64)
95% CI of LS mean	(88.43, 95.00)
Absolute Change at Week 16 (MMRM)	
n	59
LS mean (SE)	7.91 (1.64)
95% CI of LS mean	(4.63, 11.19)
Week 24	
n	62
Mean (SD)	88.71 (19.03)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 24	
n	59
Mean (SD)	5.27 (25.05)
Week 24 (MMRM)	
n	62
LS mean (SE)	89.08 (2.38)
95% CI of LS mean	(84.31, 93.84)
Absolute Change at Week 24 (MMRM)	
n	59
LS mean (SE)	5.27 (2.38)
95% CI of LS mean	(0.51, 10.04)
Absolute Change through Week 24 (MMRM)	
n	59
LS mean (SE)	6.59 (1.74)
95% CI of LS mean	(3.10, 10.08)
P-value	0.0004

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	77.78 (27.22)
Week 4 (MMRM)	
n	10
LS mean (SE)	88.89 (5.50)
95% CI of LS mean	(77.16, 100.61)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	11.11 (5.50)
95% CI of LS mean	(-0.61, 22.84)
Week 8 (MMRM)	
n	10
LS mean (SE)	81.11 (5.50)
95% CI of LS mean	(69.39, 92.84)
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	3.33 (5.50)
95% CI of LS mean	(-8.39, 15.06)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 12 (MMRM)	
n	10
LS mean (SE)	86.67 (5.50)
95% CI of LS mean	(74.94, 98.39)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	8.89 (5.50)
95% CI of LS mean	(-2.84, 20.61)
Week 16 (MMRM)	
n	10
LS mean (SE)	87.78 (5.50)
95% CI of LS mean	(76.05, 99.50)
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	10.00 (5.50)
95% CI of LS mean	(-1.73, 21.73)
Week 24	
n	10
Mean (SD)	83.33 (32.81)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 24	
n	10
Mean (SD)	5.56 (19.77)
Week 24 (MMRM)	
n	10
LS mean (SE)	83.33 (5.50)
95% CI of LS mean	(71.61, 95.06)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	5.56 (5.50)
95% CI of LS mean	(-6.17, 17.28)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	7.78 (4.90)
95% CI of LS mean	(-3.18, 18.73)
P-value	0.1442

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	41
Mean (SD)	79.67 (22.21)
Week 4 (MMRM)	
n	42
LS mean (SE)	78.86 (3.64)
95% CI of LS mean	(71.49, 86.24)
Absolute Change at Week 4 (MMRM)	
n	41
LS mean (SE)	-0.81 (3.64)
95% CI of LS mean	(-8.19, 6.56)
Week 8 (MMRM)	
n	42
LS mean (SE)	78.05 (3.54)
95% CI of LS mean	(70.90, 85.20)
Absolute Change at Week 8 (MMRM)	
n	41
LS mean (SE)	-1.63 (3.54)
95% CI of LS mean	(-8.78, 5.53)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 12 (MMRM)	
n	41
LS mean (SE)	82.00 (3.00)
95% CI of LS mean	(75.92, 88.09)
Absolute Change at Week 12 (MMRM)	
n	40
LS mean (SE)	2.33 (3.00)
95% CI of LS mean	(-3.76, 8.41)
Week 16 (MMRM)	
n	42
LS mean (SE)	84.55 (3.22)
95% CI of LS mean	(78.03, 91.08)
Absolute Change at Week 16 (MMRM)	
n	41
LS mean (SE)	4.88 (3.22)
95% CI of LS mean	(-1.64, 11.40)
Week 24	
n	44
Mean (SD)	87.12 (20.61)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 24	
n	41
Mean (SD)	8.13 (26.65)
Week 24 (MMRM)	
n	44
LS mean (SE)	87.80 (3.29)
95% CI of LS mean	(81.13, 94.48)
Absolute Change at Week 24 (MMRM)	
n	41
LS mean (SE)	8.13 (3.29)
95% CI of LS mean	(1.45, 14.81)
Absolute Change through Week 24 (MMRM)	
n	41
LS mean (SE)	6.50 (2.76)
95% CI of LS mean	(0.91, 12.09)
P-value	0.0238

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	33
Mean (SD)	79.80 (20.31)
Week 4 (MMRM)	
n	33
LS mean (SE)	75.76 (4.88)
95% CI of LS mean	(65.81, 85.70)
Absolute Change at Week 4 (MMRM)	
n	33
LS mean (SE)	-4.04 (4.88)
95% CI of LS mean	(-13.99, 5.90)
Week 8 (MMRM)	
n	33
LS mean (SE)	81.82 (4.05)
95% CI of LS mean	(73.57, 90.07)
Absolute Change at Week 8 (MMRM)	
n	33
LS mean (SE)	2.02 (4.05)
95% CI of LS mean	(-6.23, 10.27)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 12 (MMRM)	
n	33
LS mean (SE)	77.78 (3.33)
95% CI of LS mean	(70.98, 84.57)
Absolute Change at Week 12 (MMRM)	
n	33
LS mean (SE)	-2.02 (3.33)
95% CI of LS mean	(-8.81, 4.77)
Week 16 (MMRM)	
n	33
LS mean (SE)	82.83 (3.67)
95% CI of LS mean	(75.33, 90.33)
Absolute Change at Week 16 (MMRM)	
n	33
LS mean (SE)	3.03 (3.67)
95% CI of LS mean	(-4.47, 10.53)
Week 24	
n	34
Mean (SD)	81.37 (23.49)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 24	
n	33
Mean (SD)	1.01 (25.66)
Week 24 (MMRM)	
n	34
LS mean (SE)	80.81 (4.04)
95% CI of LS mean	(72.56, 89.05)
Absolute Change at Week 24 (MMRM)	
n	33
LS mean (SE)	1.01 (4.04)
95% CI of LS mean	(-7.24, 9.26)
Absolute Change through Week 24 (MMRM)	
n	33
LS mean (SE)	2.02 (3.11)
95% CI of LS mean	(-4.32, 8.36)
P-value	0.5206

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	80.85 (22.78)
Week 4 (MMRM)	
n	47
LS mean (SE)	76.60 (4.08)
95% CI of LS mean	(68.38, 84.81)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	-4.26 (4.08)
95% CI of LS mean	(-12.47, 3.96)
Week 8 (MMRM)	
n	47
LS mean (SE)	77.30 (3.55)
95% CI of LS mean	(70.16, 84.45)
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	-3.55 (3.55)
95% CI of LS mean	(-10.69, 3.60)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 12 (MMRM)	
n	47
LS mean (SE)	79.43 (2.91)
95% CI of LS mean	(73.56, 85.30)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	-1.42 (2.91)
95% CI of LS mean	(-7.29, 4.45)
Week 16 (MMRM)	
n	47
LS mean (SE)	79.43 (3.32)
95% CI of LS mean	(72.74, 86.13)
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	-1.42 (3.32)
95% CI of LS mean	(-8.11, 5.28)
Week 24	
n	47
Mean (SD)	82.98 (22.92)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 24	
n	47
Mean (SD)	2.13 (26.38)
Week 24 (MMRM)	
n	47
LS mean (SE)	82.98 (3.17)
95% CI of LS mean	(76.60, 89.36)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	2.13 (3.17)
95% CI of LS mean	(-4.25, 8.50)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	0.35 (2.77)
95% CI of LS mean	(-5.22, 5.93)
P-value	0.8986

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	27
Mean (SD)	77.78 (18.49)
Week 4 (MMRM)	
n	28
LS mean (SE)	79.01 (4.72)
95% CI of LS mean	(69.17, 88.86)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	1.23 (4.72)
95% CI of LS mean	(-8.61, 11.08)
Week 8 (MMRM)	
n	28
LS mean (SE)	83.95 (4.20)
95% CI of LS mean	(75.20, 92.70)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	6.17 (4.20)
95% CI of LS mean	(-2.58, 14.93)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 12 (MMRM)	
n	27
LS mean (SE)	80.90 (3.45)
95% CI of LS mean	(73.74, 88.06)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	3.12 (3.45)
95% CI of LS mean	(-4.04, 10.28)
Week 16 (MMRM)	
n	28
LS mean (SE)	91.36 (2.89)
95% CI of LS mean	(85.41, 97.31)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	13.58 (2.89)
95% CI of LS mean	(7.63, 19.53)
Week 24	
n	31
Mean (SD)	87.10 (20.51)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 24	
n	27
Mean (SD)	9.88 (25.84)
Week 24 (MMRM)	
n	31
LS mean (SE)	87.65 (4.05)
95% CI of LS mean	(79.33, 95.97)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	9.88 (4.05)
95% CI of LS mean	(1.56, 18.20)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	11.73 (2.56)
95% CI of LS mean	(6.45, 17.01)
P-value	0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	58
Mean (SD)	79.31 (22.36)
Week 4 (MMRM)	
n	59
LS mean (SE)	75.29 (3.49)
95% CI of LS mean	(68.30, 82.27)
Absolute Change at Week 4 (MMRM)	
n	58
LS mean (SE)	-4.02 (3.49)
95% CI of LS mean	(-11.01, 2.96)
Week 8 (MMRM)	
n	59
LS mean (SE)	78.74 (3.07)
95% CI of LS mean	(72.58, 84.89)
Absolute Change at Week 8 (MMRM)	
n	58
LS mean (SE)	-0.57 (3.07)
95% CI of LS mean	(-6.73, 5.58)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 12 (MMRM)	
n	58
LS mean (SE)	80.91 (2.31)
95% CI of LS mean	(76.28, 85.54)
Absolute Change at Week 12 (MMRM)	
n	57
LS mean (SE)	1.60 (2.31)
95% CI of LS mean	(-3.03, 6.23)
Week 16 (MMRM)	
n	59
LS mean (SE)	83.33 (2.71)
95% CI of LS mean	(77.90, 88.76)
Absolute Change at Week 16 (MMRM)	
n	58
LS mean (SE)	4.02 (2.71)
95% CI of LS mean	(-1.41, 9.45)
Week 24	
n	62
Mean (SD)	86.02 (21.38)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 24	
n	58
Mean (SD)	6.90 (26.31)
Week 24 (MMRM)	
n	62
LS mean (SE)	86.21 (2.76)
95% CI of LS mean	(80.67, 91.74)
Absolute Change at Week 24 (MMRM)	
n	58
LS mean (SE)	6.90 (2.76)
95% CI of LS mean	(1.36, 12.43)
Absolute Change through Week 24 (MMRM)	
n	58
LS mean (SE)	5.46 (2.18)
95% CI of LS mean	(1.09, 9.83)
P-value	0.0152

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	83.33 (17.57)
Week 4 (MMRM)	
n	10
LS mean (SE)	90.00 (6.99)
95% CI of LS mean	(73.39, 106.61)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	6.67 (6.99)
95% CI of LS mean	(-9.94, 23.28)
Week 8 (MMRM)	
n	10
LS mean (SE)	86.67 (7.51)
95% CI of LS mean	(69.08, 104.26)
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	3.33 (7.51)
95% CI of LS mean	(-14.26, 20.92)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 12 (MMRM)	
n	10
LS mean (SE)	83.33 (7.28)
95% CI of LS mean	(66.01, 100.66)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	0.00 (7.28)
95% CI of LS mean	(-17.33, 17.33)
Week 16 (MMRM)	
n	10
LS mean (SE)	96.67 (3.02)
95% CI of LS mean	(89.66, 103.67)
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	13.33 (3.02)
95% CI of LS mean	(6.33, 20.34)
Week 24	
n	10
Mean (SD)	90.00 (16.10)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 24	
n	10
Mean (SD)	6.67 (21.08)
Week 24 (MMRM)	
n	10
LS mean (SE)	90.00 (5.28)
95% CI of LS mean	(77.52, 102.48)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	6.67 (5.28)
95% CI of LS mean	(-5.81, 19.15)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	10.00 (2.72)
95% CI of LS mean	(2.21, 17.79)
P-value	0.0242

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	42
Mean (SD)	80.95 (23.06)
Week 4 (MMRM)	
n	42
LS mean (SE)	84.66 (2.21)
95% CI of LS mean	(80.19, 89.12)
Absolute Change at Week 4 (MMRM)	
n	42
LS mean (SE)	3.70 (2.21)
95% CI of LS mean	(-0.76, 8.17)
Week 8 (MMRM)	
n	42
LS mean (SE)	82.01 (2.67)
95% CI of LS mean	(76.60, 87.42)
Absolute Change at Week 8 (MMRM)	
n	42
LS mean (SE)	1.06 (2.67)
95% CI of LS mean	(-4.35, 6.47)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 12 (MMRM)	
n	41
LS mean (SE)	84.08 (3.10)
95% CI of LS mean	(77.83, 90.34)
Absolute Change at Week 12 (MMRM)	
n	41
LS mean (SE)	3.13 (3.10)
95% CI of LS mean	(-3.13, 9.39)
Week 16 (MMRM)	
n	42
LS mean (SE)	83.07 (3.31)
95% CI of LS mean	(76.38, 89.76)
Absolute Change at Week 16 (MMRM)	
n	42
LS mean (SE)	2.12 (3.31)
95% CI of LS mean	(-4.57, 8.80)
Week 24	
n	44
Mean (SD)	88.89 (19.76)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 24	
n	42
Mean (SD)	7.41 (16.40)
Week 24 (MMRM)	
n	44
LS mean (SE)	88.36 (2.22)
95% CI of LS mean	(83.87, 92.85)
Absolute Change at Week 24 (MMRM)	
n	42
LS mean (SE)	7.41 (2.22)
95% CI of LS mean	(2.92, 11.90)
Absolute Change through Week 24 (MMRM)	
n	42
LS mean (SE)	4.76 (2.32)
95% CI of LS mean	(0.07, 9.46)
P-value	0.0469

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	33
Mean (SD)	82.15 (19.43)
Week 4 (MMRM)	
n	33
LS mean (SE)	78.11 (3.63)
95% CI of LS mean	(70.71, 85.52)
Absolute Change at Week 4 (MMRM)	
n	33
LS mean (SE)	-4.04 (3.63)
95% CI of LS mean	(-11.45, 3.37)
Week 8 (MMRM)	
n	33
LS mean (SE)	77.10 (3.65)
95% CI of LS mean	(69.67, 84.54)
Absolute Change at Week 8 (MMRM)	
n	33
LS mean (SE)	-5.05 (3.65)
95% CI of LS mean	(-12.49, 2.39)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 12 (MMRM)	
n	33
LS mean (SE)	82.49 (3.23)
95% CI of LS mean	(75.91, 89.08)
Absolute Change at Week 12 (MMRM)	
n	33
LS mean (SE)	0.34 (3.23)
95% CI of LS mean	(-6.25, 6.92)
Week 16 (MMRM)	
n	33
LS mean (SE)	86.20 (2.54)
95% CI of LS mean	(81.01, 91.38)
Absolute Change at Week 16 (MMRM)	
n	33
LS mean (SE)	4.04 (2.54)
95% CI of LS mean	(-1.14, 9.22)
Week 24	
n	34
Mean (SD)	88.89 (16.18)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 24	
n	33
Mean (SD)	7.07 (18.39)
Week 24 (MMRM)	
n	34
LS mean (SE)	89.23 (2.55)
95% CI of LS mean	(84.01, 94.44)
Absolute Change at Week 24 (MMRM)	
n	33
LS mean (SE)	7.07 (2.55)
95% CI of LS mean	(1.86, 12.28)
Absolute Change through Week 24 (MMRM)	
n	33
LS mean (SE)	5.56 (2.21)
95% CI of LS mean	(1.04, 10.07)
P-value	0.0176

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	78.01 (23.57)
Week 4 (MMRM)	
n	47
LS mean (SE)	79.20 (2.61)
95% CI of LS mean	(73.93, 84.46)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	1.18 (2.61)
95% CI of LS mean	(-4.08, 6.44)
Week 8 (MMRM)	
n	47
LS mean (SE)	79.67 (2.64)
95% CI of LS mean	(74.35, 84.99)
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	1.65 (2.64)
95% CI of LS mean	(-3.66, 6.97)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 12 (MMRM)	
n	47
LS mean (SE)	82.51 (2.96)
95% CI of LS mean	(76.54, 88.47)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	4.49 (2.96)
95% CI of LS mean	(-1.47, 10.45)
Week 16 (MMRM)	
n	47
LS mean (SE)	81.56 (3.21)
95% CI of LS mean	(75.09, 88.03)
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	3.55 (3.21)
95% CI of LS mean	(-2.92, 10.02)
Week 24	
n	47
Mean (SD)	88.42 (19.10)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 24	
n	47
Mean (SD)	10.40 (18.01)
Week 24 (MMRM)	
n	47
LS mean (SE)	88.42 (2.15)
95% CI of LS mean	(84.08, 92.75)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	10.40 (2.15)
95% CI of LS mean	(6.06, 14.74)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	6.97 (2.31)
95% CI of LS mean	(2.33, 11.62)
P-value	0.0042

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	28
Mean (SD)	87.30 (15.92)
Week 4 (MMRM)	
n	28
LS mean (SE)	86.11 (3.39)
95% CI of LS mean	(79.16, 93.06)
Absolute Change at Week 4 (MMRM)	
n	28
LS mean (SE)	-1.19 (3.39)
95% CI of LS mean	(-8.14, 5.76)
Week 8 (MMRM)	
n	28
LS mean (SE)	80.16 (4.08)
95% CI of LS mean	(71.75, 88.57)
Absolute Change at Week 8 (MMRM)	
n	28
LS mean (SE)	-7.14 (4.08)
95% CI of LS mean	(-15.55, 1.27)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 12 (MMRM)	
n	27
LS mean (SE)	84.88 (3.44)
95% CI of LS mean	(77.79, 91.96)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	-2.43 (3.44)
95% CI of LS mean	(-9.51, 4.66)
Week 16 (MMRM)	
n	28
LS mean (SE)	89.29 (2.28)
95% CI of LS mean	(84.59, 93.98)
Absolute Change at Week 16 (MMRM)	
n	28
LS mean (SE)	1.98 (2.28)
95% CI of LS mean	(-2.71, 6.68)
Week 24	
n	31
Mean (SD)	89.61 (16.96)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 24	
n	28
Mean (SD)	1.98 (14.52)
Week 24 (MMRM)	
n	31
LS mean (SE)	89.29 (2.65)
95% CI of LS mean	(83.84, 94.73)
Absolute Change at Week 24 (MMRM)	
n	28
LS mean (SE)	1.98 (2.65)
95% CI of LS mean	(-3.46, 7.43)
Absolute Change through Week 24 (MMRM)	
n	28
LS mean (SE)	1.98 (2.11)
95% CI of LS mean	(-2.37, 6.33)
P-value	0.3569

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	59
Mean (SD)	82.11 (20.63)
Week 4 (MMRM)	
n	59
LS mean (SE)	81.92 (2.28)
95% CI of LS mean	(77.35, 86.49)
Absolute Change at Week 4 (MMRM)	
n	59
LS mean (SE)	-0.19 (2.28)
95% CI of LS mean	(-4.76, 4.39)
Week 8 (MMRM)	
n	59
LS mean (SE)	82.49 (1.61)
95% CI of LS mean	(79.26, 85.71)
Absolute Change at Week 8 (MMRM)	
n	59
LS mean (SE)	0.38 (1.61)
95% CI of LS mean	(-2.85, 3.60)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 12 (MMRM)	
n	58
LS mean (SE)	87.16 (2.01)
95% CI of LS mean	(83.13, 91.19)
Absolute Change at Week 12 (MMRM)	
n	58
LS mean (SE)	5.05 (2.01)
95% CI of LS mean	(1.02, 9.08)
Week 16 (MMRM)	
n	59
LS mean (SE)	87.38 (2.21)
95% CI of LS mean	(82.96, 91.81)
Absolute Change at Week 16 (MMRM)	
n	59
LS mean (SE)	5.27 (2.21)
95% CI of LS mean	(0.85, 9.70)
Week 24	
n	62
Mean (SD)	89.07 (18.71)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 24	
n	59
Mean (SD)	6.78 (15.72)
Week 24 (MMRM)	
n	62
LS mean (SE)	88.89 (1.82)
95% CI of LS mean	(85.25, 92.52)
Absolute Change at Week 24 (MMRM)	
n	59
LS mean (SE)	6.78 (1.82)
95% CI of LS mean	(3.14, 10.41)
Absolute Change through Week 24 (MMRM)	
n	59
LS mean (SE)	6.03 (1.75)
95% CI of LS mean	(2.53, 9.53)
P-value	0.0011

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	87.78 (17.72)
Week 4 (MMRM)	
n	10
LS mean (SE)	85.56 (4.62)
95% CI of LS mean	(76.09, 95.03)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	-2.22 (4.62)
95% CI of LS mean	(-11.69, 7.25)
Week 8 (MMRM)	
n	10
LS mean (SE)	85.56 (4.62)
95% CI of LS mean	(76.09, 95.03)
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	-2.22 (4.62)
95% CI of LS mean	(-11.69, 7.25)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 12 (MMRM)	
n	10
LS mean (SE)	86.67 (4.62)
95% CI of LS mean	(77.20, 96.14)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	-1.11 (4.62)
95% CI of LS mean	(-10.58, 8.36)
Week 16 (MMRM)	
n	10
LS mean (SE)	85.56 (4.62)
95% CI of LS mean	(76.09, 95.03)
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	-2.22 (4.62)
95% CI of LS mean	(-11.69, 7.25)
Week 24	
n	10
Mean (SD)	94.44 (10.80)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 24	
n	10
Mean (SD)	6.67 (21.72)
Week 24 (MMRM)	
n	10
LS mean (SE)	94.44 (4.62)
95% CI of LS mean	(84.97, 103.91)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	6.67 (4.62)
95% CI of LS mean	(-2.80, 16.14)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	2.22 (3.72)
95% CI of LS mean	(-5.74, 10.18)
P-value	0.5599

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	42
Mean (SD)	78.77 (12.84)
Week 4 (MMRM)	
n	42
LS mean (SE)	79.96 (1.87)
95% CI of LS mean	(76.17, 83.75)
Absolute Change at Week 4 (MMRM)	
n	42
LS mean (SE)	1.19 (1.87)
95% CI of LS mean	(-2.60, 4.98)
Week 8 (MMRM)	
n	42
LS mean (SE)	81.85 (1.67)
95% CI of LS mean	(78.46, 85.23)
Absolute Change at Week 8 (MMRM)	
n	42
LS mean (SE)	3.08 (1.67)
95% CI of LS mean	(-0.31, 6.46)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 12 (MMRM)	
n	41
LS mean (SE)	83.48 (2.05)
95% CI of LS mean	(79.34, 87.62)
Absolute Change at Week 12 (MMRM)	
n	41
LS mean (SE)	4.71 (2.05)
95% CI of LS mean	(0.57, 8.85)
Week 16 (MMRM)	
n	42
LS mean (SE)	84.13 (2.25)
95% CI of LS mean	(79.57, 88.68)
Absolute Change at Week 16 (MMRM)	
n	42
LS mean (SE)	5.36 (2.25)
95% CI of LS mean	(0.80, 9.91)
Week 24	
n	44
Mean (SD)	81.34 (14.83)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 24	
n	42
Mean (SD)	3.27 (10.95)
Week 24 (MMRM)	
n	44
LS mean (SE)	82.04 (1.70)
95% CI of LS mean	(78.61, 85.48)
Absolute Change at Week 24 (MMRM)	
n	42
LS mean (SE)	3.27 (1.70)
95% CI of LS mean	(-0.16, 6.71)
Absolute Change through Week 24 (MMRM)	
n	42
LS mean (SE)	4.32 (1.80)
95% CI of LS mean	(0.67, 7.96)
P-value	0.0216

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	33
Mean (SD)	73.61 (16.46)
Week 4 (MMRM)	
n	33
LS mean (SE)	72.13 (2.10)
95% CI of LS mean	(67.85, 76.41)
Absolute Change at Week 4 (MMRM)	
n	33
LS mean (SE)	-1.48 (2.10)
95% CI of LS mean	(-5.76, 2.80)
Week 8 (MMRM)	
n	33
LS mean (SE)	72.98 (2.40)
95% CI of LS mean	(68.09, 77.87)
Absolute Change at Week 8 (MMRM)	
n	33
LS mean (SE)	-0.63 (2.40)
95% CI of LS mean	(-5.53, 4.26)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 12 (MMRM)	
n	33
LS mean (SE)	74.62 (2.48)
95% CI of LS mean	(69.56, 79.68)
Absolute Change at Week 12 (MMRM)	
n	33
LS mean (SE)	1.01 (2.48)
95% CI of LS mean	(-4.05, 6.07)
Week 16 (MMRM)	
n	33
LS mean (SE)	75.25 (2.42)
95% CI of LS mean	(70.32, 80.18)
Absolute Change at Week 16 (MMRM)	
n	33
LS mean (SE)	1.64 (2.42)
95% CI of LS mean	(-3.29, 6.57)
Week 24	
n	34
Mean (SD)	77.82 (15.24)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 24	
n	33
Mean (SD)	4.42 (14.13)
Week 24 (MMRM)	
n	34
LS mean (SE)	78.03 (2.10)
95% CI of LS mean	(73.75, 82.31)
Absolute Change at Week 24 (MMRM)	
n	33
LS mean (SE)	4.42 (2.10)
95% CI of LS mean	(0.14, 8.70)
Absolute Change through Week 24 (MMRM)	
n	33
LS mean (SE)	3.03 (2.00)
95% CI of LS mean	(-1.06, 7.12)
P-value	0.1406

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	72.96 (14.48)
Week 4 (MMRM)	
n	47
LS mean (SE)	72.54 (1.98)
95% CI of LS mean	(68.56, 76.53)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	-0.42 (1.98)
95% CI of LS mean	(-4.41, 3.57)
Week 8 (MMRM)	
n	47
LS mean (SE)	75.71 (1.92)
95% CI of LS mean	(71.84, 79.58)
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	2.75 (1.92)
95% CI of LS mean	(-1.13, 6.62)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 12 (MMRM)	
n	47
LS mean (SE)	77.84 (2.02)
95% CI of LS mean	(73.77, 81.90)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	4.88 (2.02)
95% CI of LS mean	(0.81, 8.94)
Week 16 (MMRM)	
n	47
LS mean (SE)	78.28 (2.28)
95% CI of LS mean	(73.68, 82.88)
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	5.32 (2.28)
95% CI of LS mean	(0.72, 9.92)
Week 24	
n	47
Mean (SD)	77.75 (15.40)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 24	
n	47
Mean (SD)	4.79 (12.04)
Week 24 (MMRM)	
n	47
LS mean (SE)	77.75 (1.69)
95% CI of LS mean	(74.33, 81.16)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	4.79 (1.69)
95% CI of LS mean	(1.37, 8.20)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	5.05 (1.79)
95% CI of LS mean	(1.44, 8.66)
P-value	0.0072

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	28
Mean (SD)	82.44 (13.19)
Week 4 (MMRM)	
n	28
LS mean (SE)	83.18 (2.14)
95% CI of LS mean	(78.79, 87.58)
Absolute Change at Week 4 (MMRM)	
n	28
LS mean (SE)	0.74 (2.14)
95% CI of LS mean	(-3.65, 5.14)
Week 8 (MMRM)	
n	28
LS mean (SE)	81.70 (2.38)
95% CI of LS mean	(76.81, 86.58)
Absolute Change at Week 8 (MMRM)	
n	28
LS mean (SE)	-0.74 (2.38)
95% CI of LS mean	(-5.63, 4.14)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 12 (MMRM)	
n	27
LS mean (SE)	82.49 (2.76)
95% CI of LS mean	(76.82, 88.17)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	0.05 (2.76)
95% CI of LS mean	(-5.62, 5.73)
Week 16 (MMRM)	
n	28
LS mean (SE)	83.48 (2.39)
95% CI of LS mean	(78.54, 88.43)
Absolute Change at Week 16 (MMRM)	
n	28
LS mean (SE)	1.04 (2.39)
95% CI of LS mean	(-3.90, 5.99)
Week 24	
n	31
Mean (SD)	82.93 (14.08)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 24	
n	28
Mean (SD)	2.08 (12.95)
Week 24 (MMRM)	
n	31
LS mean (SE)	84.52 (2.21)
95% CI of LS mean	(79.97, 89.08)
Absolute Change at Week 24 (MMRM)	
n	28
LS mean (SE)	2.08 (2.21)
95% CI of LS mean	(-2.47, 6.64)
Absolute Change through Week 24 (MMRM)	
n	28
LS mean (SE)	1.56 (2.08)
95% CI of LS mean	(-2.74, 5.86)
P-value	0.4602

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	59
Mean (SD)	75.99 (14.27)
Week 4 (MMRM)	
n	59
LS mean (SE)	76.41 (1.61)
95% CI of LS mean	(73.18, 79.64)
Absolute Change at Week 4 (MMRM)	
n	59
LS mean (SE)	0.42 (1.61)
95% CI of LS mean	(-2.81, 3.65)
Week 8 (MMRM)	
n	59
LS mean (SE)	78.39 (1.70)
95% CI of LS mean	(74.98, 81.80)
Absolute Change at Week 8 (MMRM)	
n	59
LS mean (SE)	2.40 (1.70)
95% CI of LS mean	(-1.00, 5.81)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 12 (MMRM)	
n	58
LS mean (SE)	79.62 (1.85)
95% CI of LS mean	(75.91, 83.32)
Absolute Change at Week 12 (MMRM)	
n	58
LS mean (SE)	3.63 (1.85)
95% CI of LS mean	(-0.07, 7.33)
Week 16 (MMRM)	
n	59
LS mean (SE)	81.57 (1.64)
95% CI of LS mean	(78.27, 84.86)
Absolute Change at Week 16 (MMRM)	
n	59
LS mean (SE)	5.58 (1.64)
95% CI of LS mean	(2.28, 8.87)
Week 24	
n	62
Mean (SD)	79.64 (14.30)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 24	
n	59
Mean (SD)	4.24 (12.46)
Week 24 (MMRM)	
n	62
LS mean (SE)	80.23 (1.43)
95% CI of LS mean	(77.36, 83.09)
Absolute Change at Week 24 (MMRM)	
n	59
LS mean (SE)	4.24 (1.43)
95% CI of LS mean	(1.38, 7.10)
Absolute Change through Week 24 (MMRM)	
n	59
LS mean (SE)	4.91 (1.35)
95% CI of LS mean	(2.21, 7.60)
P-value	0.0006

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	77.92 (19.15)
Week 4 (MMRM)	
n	10
LS mean (SE)	80.54 (3.02)
95% CI of LS mean	(73.67, 87.40)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	2.62 (3.02)
95% CI of LS mean	(-4.25, 9.48)
Week 8 (MMRM)	
n	10
LS mean (SE)	79.58 (2.84)
95% CI of LS mean	(73.15, 86.01)
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	1.67 (2.84)
95% CI of LS mean	(-4.76, 8.10)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 12 (MMRM)	
n	10
LS mean (SE)	82.50 (2.02)
95% CI of LS mean	(77.82, 87.18)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	4.58 (2.02)
95% CI of LS mean	(-0.09, 9.26)
Week 16 (MMRM)	
n	10
LS mean (SE)	80.42 (3.32)
95% CI of LS mean	(72.89, 87.94)
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	2.50 (3.32)
95% CI of LS mean	(-5.03, 10.03)
Week 24	
n	10
Mean (SD)	84.58 (19.74)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 24	
n	10
Mean (SD)	6.67 (11.49)
Week 24 (MMRM)	
n	10
LS mean (SE)	84.58 (4.11)
95% CI of LS mean	(75.23, 93.94)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	6.67 (4.11)
95% CI of LS mean	(-2.69, 16.02)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	4.58 (3.45)
95% CI of LS mean	(-3.27, 12.44)
P-value	0.2184

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	42
Mean (SD)	88.36 (11.88)
Week 4 (MMRM)	
n	42
LS mean (SE)	86.90 (1.85)
95% CI of LS mean	(83.17, 90.64)
Absolute Change at Week 4 (MMRM)	
n	42
LS mean (SE)	-1.46 (1.85)
95% CI of LS mean	(-5.19, 2.28)
Week 8 (MMRM)	
n	42
LS mean (SE)	84.79 (2.57)
95% CI of LS mean	(79.59, 89.99)
Absolute Change at Week 8 (MMRM)	
n	42
LS mean (SE)	-3.57 (2.57)
95% CI of LS mean	(-8.77, 1.63)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 12 (MMRM)	
n	41
LS mean (SE)	86.65 (1.98)
95% CI of LS mean	(82.65, 90.64)
Absolute Change at Week 12 (MMRM)	
n	41
LS mean (SE)	-1.71 (1.98)
95% CI of LS mean	(-5.71, 2.28)
Week 16 (MMRM)	
n	42
LS mean (SE)	87.57 (2.49)
95% CI of LS mean	(82.54, 92.59)
Absolute Change at Week 16 (MMRM)	
n	42
LS mean (SE)	-0.79 (2.49)
95% CI of LS mean	(-5.82, 4.23)
Week 24	
n	44
Mean (SD)	90.40 (15.91)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 24	
n	42
Mean (SD)	1.72 (15.15)
Week 24 (MMRM)	
n	44
LS mean (SE)	90.08 (2.25)
95% CI of LS mean	(85.53, 94.63)
Absolute Change at Week 24 (MMRM)	
n	42
LS mean (SE)	1.72 (2.25)
95% CI of LS mean	(-2.83, 6.27)
Absolute Change through Week 24 (MMRM)	
n	42
LS mean (SE)	0.46 (1.92)
95% CI of LS mean	(-3.42, 4.34)
P-value	0.8106

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	33
Mean (SD)	85.86 (14.37)
Week 4 (MMRM)	
n	33
LS mean (SE)	87.04 (2.22)
95% CI of LS mean	(82.49, 91.58)
Absolute Change at Week 4 (MMRM)	
n	33
LS mean (SE)	1.18 (2.22)
95% CI of LS mean	(-3.37, 5.72)
Week 8 (MMRM)	
n	33
LS mean (SE)	86.43 (2.52)
95% CI of LS mean	(81.29, 91.57)
Absolute Change at Week 8 (MMRM)	
n	33
LS mean (SE)	0.57 (2.52)
95% CI of LS mean	(-4.57, 5.72)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 12 (MMRM)	
n	33
LS mean (SE)	85.86 (3.33)
95% CI of LS mean	(79.08, 92.64)
Absolute Change at Week 12 (MMRM)	
n	33
LS mean (SE)	0.00 (3.33)
95% CI of LS mean	(-6.78, 6.78)
Week 16 (MMRM)	
n	33
LS mean (SE)	89.73 (2.13)
95% CI of LS mean	(85.39, 94.07)
Absolute Change at Week 16 (MMRM)	
n	33
LS mean (SE)	3.87 (2.13)
95% CI of LS mean	(-0.47, 8.22)
Week 24	
n	34
Mean (SD)	90.36 (12.48)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 24	
n	33
Mean (SD)	5.39 (12.99)
Week 24 (MMRM)	
n	34
LS mean (SE)	91.25 (1.76)
95% CI of LS mean	(87.64, 94.85)
Absolute Change at Week 24 (MMRM)	
n	33
LS mean (SE)	5.39 (1.76)
95% CI of LS mean	(1.79, 8.99)
Absolute Change through Week 24 (MMRM)	
n	33
LS mean (SE)	4.63 (1.75)
95% CI of LS mean	(1.05, 8.21)
P-value	0.0129

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	86.05 (12.79)
Week 4 (MMRM)	
n	47
LS mean (SE)	85.22 (1.90)
95% CI of LS mean	(81.40, 89.05)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	-0.83 (1.90)
95% CI of LS mean	(-4.65, 3.00)
Week 8 (MMRM)	
n	47
LS mean (SE)	84.80 (2.22)
95% CI of LS mean	(80.32, 89.28)
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	-1.25 (2.22)
95% CI of LS mean	(-5.74, 3.23)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 12 (MMRM)	
n	47
LS mean (SE)	86.88 (2.19)
95% CI of LS mean	(82.46, 91.29)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	0.83 (2.19)
95% CI of LS mean	(-3.59, 5.24)
Week 16 (MMRM)	
n	47
LS mean (SE)	89.95 (2.03)
95% CI of LS mean	(85.86, 94.05)
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	3.90 (2.03)
95% CI of LS mean	(-0.19, 7.99)
Week 24	
n	47
Mean (SD)	89.48 (16.27)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 24	
n	47
Mean (SD)	3.43 (16.49)
Week 24 (MMRM)	
n	47
LS mean (SE)	89.48 (2.24)
95% CI of LS mean	(84.96, 94.00)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	3.43 (2.24)
95% CI of LS mean	(-1.09, 7.95)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	3.66 (1.81)
95% CI of LS mean	(0.02, 7.31)
P-value	0.0490

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	28
Mean (SD)	89.29 (13.35)
Week 4 (MMRM)	
n	28
LS mean (SE)	89.88 (1.67)
95% CI of LS mean	(86.45, 93.31)
Absolute Change at Week 4 (MMRM)	
n	28
LS mean (SE)	0.60 (1.67)
95% CI of LS mean	(-2.84, 4.03)
Week 8 (MMRM)	
n	28
LS mean (SE)	86.71 (3.12)
95% CI of LS mean	(80.30, 93.11)
Absolute Change at Week 8 (MMRM)	
n	28
LS mean (SE)	-2.58 (3.12)
95% CI of LS mean	(-8.98, 3.82)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 12 (MMRM)	
n	27
LS mean (SE)	85.76 (3.34)
95% CI of LS mean	(78.89, 92.63)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	-3.53 (3.34)
95% CI of LS mean	(-10.40, 3.34)
Week 16 (MMRM)	
n	28
LS mean (SE)	86.11 (2.89)
95% CI of LS mean	(80.17, 92.05)
Absolute Change at Week 16 (MMRM)	
n	28
LS mean (SE)	-3.17 (2.89)
95% CI of LS mean	(-9.12, 2.77)
Week 24	
n	31
Mean (SD)	91.76 (11.19)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 24	
n	28
Mean (SD)	3.17 (9.73)
Week 24 (MMRM)	
n	31
LS mean (SE)	92.46 (1.32)
95% CI of LS mean	(89.74, 95.18)
Absolute Change at Week 24 (MMRM)	
n	28
LS mean (SE)	3.17 (1.32)
95% CI of LS mean	(0.45, 5.89)
Absolute Change through Week 24 (MMRM)	
n	28
LS mean (SE)	0.00 (1.89)
95% CI of LS mean	(-3.89, 3.89)
P-value	>0.9999

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	59
Mean (SD)	85.12 (13.59)
Week 4 (MMRM)	
n	59
LS mean (SE)	85.97 (1.56)
95% CI of LS mean	(82.84, 89.10)
Absolute Change at Week 4 (MMRM)	
n	59
LS mean (SE)	0.85 (1.56)
95% CI of LS mean	(-2.28, 3.98)
Week 8 (MMRM)	
n	59
LS mean (SE)	84.78 (1.92)
95% CI of LS mean	(80.93, 88.63)
Absolute Change at Week 8 (MMRM)	
n	59
LS mean (SE)	-0.34 (1.92)
95% CI of LS mean	(-4.19, 3.51)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 12 (MMRM)	
n	58
LS mean (SE)	87.29 (1.63)
95% CI of LS mean	(84.04, 90.55)
Absolute Change at Week 12 (MMRM)	
n	58
LS mean (SE)	2.17 (1.63)
95% CI of LS mean	(-1.08, 5.43)
Week 16 (MMRM)	
n	59
LS mean (SE)	88.32 (1.82)
95% CI of LS mean	(84.68, 91.96)
Absolute Change at Week 16 (MMRM)	
n	59
LS mean (SE)	3.20 (1.82)
95% CI of LS mean	(-0.44, 6.84)
Week 24	
n	62
Mean (SD)	89.52 (15.23)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 24	
n	59
Mean (SD)	4.61 (14.63)
Week 24 (MMRM)	
n	62
LS mean (SE)	89.74 (1.74)
95% CI of LS mean	(86.26, 93.22)
Absolute Change at Week 24 (MMRM)	
n	59
LS mean (SE)	4.61 (1.74)
95% CI of LS mean	(1.14, 8.09)
Absolute Change through Week 24 (MMRM)	
n	59
LS mean (SE)	3.91 (1.44)
95% CI of LS mean	(1.03, 6.79)
P-value	0.0088

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	94.44 (7.41)
Week 4 (MMRM)	
n	10
LS mean (SE)	94.44 (4.54)
95% CI of LS mean	(84.36, 104.53)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	0.00 (4.54)
95% CI of LS mean	(-10.08, 10.08)
Week 8 (MMRM)	
n	10
LS mean (SE)	92.78 (4.54)
95% CI of LS mean	(82.69, 102.86)
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	-1.67 (4.54)
95% CI of LS mean	(-11.75, 8.42)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 12 (MMRM)	
n	10
LS mean (SE)	89.44 (4.54)
95% CI of LS mean	(79.36, 99.53)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	-5.00 (4.54)
95% CI of LS mean	(-15.08, 5.08)
Week 16 (MMRM)	
n	10
LS mean (SE)	92.78 (4.54)
95% CI of LS mean	(82.69, 102.86)
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	-1.67 (4.54)
95% CI of LS mean	(-11.75, 8.42)
Week 24	
n	10
Mean (SD)	94.44 (12.83)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 24	
n	10
Mean (SD)	0.00 (14.10)
Week 24 (MMRM)	
n	10
LS mean (SE)	94.44 (4.54)
95% CI of LS mean	(84.36, 104.53)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	0.00 (4.54)
95% CI of LS mean	(-10.08, 10.08)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	-0.83 (4.28)
95% CI of LS mean	(-10.68, 9.01)
P-value	0.8505

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	42
Mean (SD)	66.33 (16.44)
Week 4 (MMRM)	
n	42
LS mean (SE)	68.82 (2.01)
95% CI of LS mean	(64.76, 72.88)
Absolute Change at Week 4 (MMRM)	
n	42
LS mean (SE)	2.49 (2.01)
95% CI of LS mean	(-1.57, 6.56)
Week 8 (MMRM)	
n	42
LS mean (SE)	67.35 (2.06)
95% CI of LS mean	(63.19, 71.51)
Absolute Change at Week 8 (MMRM)	
n	42
LS mean (SE)	1.02 (2.06)
95% CI of LS mean	(-3.14, 5.18)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 12 (MMRM)	
n	41
LS mean (SE)	72.14 (2.20)
95% CI of LS mean	(67.70, 76.59)
Absolute Change at Week 12 (MMRM)	
n	41
LS mean (SE)	5.82 (2.20)
95% CI of LS mean	(1.37, 10.26)
Week 16 (MMRM)	
n	42
LS mean (SE)	74.72 (2.15)
95% CI of LS mean	(70.38, 79.05)
Absolute Change at Week 16 (MMRM)	
n	42
LS mean (SE)	8.39 (2.15)
95% CI of LS mean	(4.06, 12.72)
Week 24	
n	44
Mean (SD)	74.89 (15.04)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 24	
n	42
Mean (SD)	9.07 (17.08)
Week 24 (MMRM)	
n	44
LS mean (SE)	75.40 (2.12)
95% CI of LS mean	(71.10, 79.69)
Absolute Change at Week 24 (MMRM)	
n	42
LS mean (SE)	9.07 (2.12)
95% CI of LS mean	(4.77, 13.37)
Absolute Change through Week 24 (MMRM)	
n	42
LS mean (SE)	8.73 (2.01)
95% CI of LS mean	(4.67, 12.79)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	33
Mean (SD)	67.82 (22.56)
Week 4 (MMRM)	
n	33
LS mean (SE)	67.24 (2.67)
95% CI of LS mean	(61.79, 72.70)
Absolute Change at Week 4 (MMRM)	
n	33
LS mean (SE)	-0.58 (2.67)
95% CI of LS mean	(-6.03, 4.88)
Week 8 (MMRM)	
n	33
LS mean (SE)	71.14 (3.26)
95% CI of LS mean	(64.50, 77.78)
Absolute Change at Week 8 (MMRM)	
n	33
LS mean (SE)	3.32 (3.26)
95% CI of LS mean	(-3.32, 9.96)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 12 (MMRM)	
n	33
LS mean (SE)	72.73 (2.76)
95% CI of LS mean	(67.09, 78.37)
Absolute Change at Week 12 (MMRM)	
n	33
LS mean (SE)	4.91 (2.76)
95% CI of LS mean	(-0.73, 10.54)
Week 16 (MMRM)	
n	33
LS mean (SE)	70.13 (3.57)
95% CI of LS mean	(62.85, 77.41)
Absolute Change at Week 16 (MMRM)	
n	33
LS mean (SE)	2.31 (3.57)
95% CI of LS mean	(-4.97, 9.59)
Week 24	
n	34
Mean (SD)	74.86 (15.96)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 24	
n	33
Mean (SD)	8.15 (23.06)
Week 24 (MMRM)	
n	34
LS mean (SE)	75.97 (2.54)
95% CI of LS mean	(70.76, 81.19)
Absolute Change at Week 24 (MMRM)	
n	33
LS mean (SE)	8.15 (2.54)
95% CI of LS mean	(2.94, 13.37)
Absolute Change through Week 24 (MMRM)	
n	33
LS mean (SE)	5.23 (2.74)
95% CI of LS mean	(-0.38, 10.84)
P-value	0.0664

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	66.36 (19.94)
Week 4 (MMRM)	
n	47
LS mean (SE)	69.20 (1.97)
95% CI of LS mean	(65.21, 73.18)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	2.84 (1.97)
95% CI of LS mean	(-1.15, 6.82)
Week 8 (MMRM)	
n	47
LS mean (SE)	69.81 (2.48)
95% CI of LS mean	(64.81, 74.80)
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	3.44 (2.48)
95% CI of LS mean	(-1.55, 8.44)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 12 (MMRM)	
n	47
LS mean (SE)	73.35 (2.25)
95% CI of LS mean	(68.82, 77.88)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	6.99 (2.25)
95% CI of LS mean	(2.46, 11.52)
Week 16 (MMRM)	
n	47
LS mean (SE)	74.47 (2.59)
95% CI of LS mean	(69.25, 79.69)
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	8.11 (2.59)
95% CI of LS mean	(2.89, 13.32)
Week 24	
n	47
Mean (SD)	76.44 (13.74)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 24	
n	47
Mean (SD)	10.08 (20.59)
Week 24 (MMRM)	
n	47
LS mean (SE)	76.44 (2.01)
95% CI of LS mean	(72.38, 80.51)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	10.08 (2.01)
95% CI of LS mean	(6.01, 14.15)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	9.09 (2.10)
95% CI of LS mean	(4.85, 13.33)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	28
Mean (SD)	68.03 (18.32)
Week 4 (MMRM)	
n	28
LS mean (SE)	66.33 (2.73)
95% CI of LS mean	(60.69, 71.96)
Absolute Change at Week 4 (MMRM)	
n	28
LS mean (SE)	-1.70 (2.73)
95% CI of LS mean	(-7.33, 3.93)
Week 8 (MMRM)	
n	28
LS mean (SE)	67.69 (2.62)
95% CI of LS mean	(62.29, 73.09)
Absolute Change at Week 8 (MMRM)	
n	28
LS mean (SE)	-0.34 (2.62)
95% CI of LS mean	(-5.74, 5.06)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 12 (MMRM)	
n	27
LS mean (SE)	70.71 (2.60)
95% CI of LS mean	(65.37, 76.06)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	2.69 (2.60)
95% CI of LS mean	(-2.66, 8.03)
Week 16 (MMRM)	
n	28
LS mean (SE)	69.73 (3.05)
95% CI of LS mean	(63.47, 75.99)
Absolute Change at Week 16 (MMRM)	
n	28
LS mean (SE)	1.70 (3.05)
95% CI of LS mean	(-4.56, 7.96)
Week 24	
n	31
Mean (SD)	72.50 (17.46)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 24	
n	28
Mean (SD)	6.29 (18.51)
Week 24 (MMRM)	
n	31
LS mean (SE)	74.32 (2.90)
95% CI of LS mean	(68.36, 80.28)
Absolute Change at Week 24 (MMRM)	
n	28
LS mean (SE)	6.29 (2.90)
95% CI of LS mean	(0.33, 12.25)
Absolute Change through Week 24 (MMRM)	
n	28
LS mean (SE)	4.00 (2.72)
95% CI of LS mean	(-1.59, 9.59)
P-value	0.1537

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	59
Mean (SD)	67.31 (17.85)
Week 4 (MMRM)	
n	59
LS mean (SE)	68.12 (1.81)
95% CI of LS mean	(64.49, 71.74)
Absolute Change at Week 4 (MMRM)	
n	59
LS mean (SE)	0.81 (1.81)
95% CI of LS mean	(-2.82, 4.43)
Week 8 (MMRM)	
n	59
LS mean (SE)	70.06 (1.71)
95% CI of LS mean	(66.62, 73.49)
Absolute Change at Week 8 (MMRM)	
n	59
LS mean (SE)	2.74 (1.71)
95% CI of LS mean	(-0.69, 6.18)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 12 (MMRM)	
n	58
LS mean (SE)	74.01 (1.82)
95% CI of LS mean	(70.36, 77.65)
Absolute Change at Week 12 (MMRM)	
n	58
LS mean (SE)	6.69 (1.82)
95% CI of LS mean	(3.04, 10.34)
Week 16 (MMRM)	
n	59
LS mean (SE)	74.01 (2.03)
95% CI of LS mean	(69.94, 78.08)
Absolute Change at Week 16 (MMRM)	
n	59
LS mean (SE)	6.70 (2.03)
95% CI of LS mean	(2.63, 10.77)
Week 24	
n	62
Mean (SD)	75.92 (14.80)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 24	
n	59
Mean (SD)	9.64 (19.23)
Week 24 (MMRM)	
n	62
LS mean (SE)	76.96 (1.83)
95% CI of LS mean	(73.29, 80.62)
Absolute Change at Week 24 (MMRM)	
n	59
LS mean (SE)	9.64 (1.83)
95% CI of LS mean	(5.98, 13.31)
Absolute Change through Week 24 (MMRM)	
n	59
LS mean (SE)	8.17 (1.74)
95% CI of LS mean	(4.68, 11.66)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	67.14 (28.87)
Week 4 (MMRM)	
n	10
LS mean (SE)	71.90 (3.63)
95% CI of LS mean	(63.62, 80.19)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	4.76 (3.63)
95% CI of LS mean	(-3.53, 13.05)
Week 8 (MMRM)	
n	10
LS mean (SE)	72.86 (8.01)
95% CI of LS mean	(54.36, 91.36)
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	5.71 (8.01)
95% CI of LS mean	(-12.79, 24.21)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 12 (MMRM)	
n	10
LS mean (SE)	72.86 (4.54)
95% CI of LS mean	(62.38, 83.34)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	5.71 (4.54)
95% CI of LS mean	(-4.77, 16.20)
Week 16 (MMRM)	
n	10
LS mean (SE)	74.29 (7.13)
95% CI of LS mean	(58.00, 90.57)
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	7.14 (7.13)
95% CI of LS mean	(-9.15, 23.43)
Week 24	
n	10
Mean (SD)	73.33 (17.56)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 24	
n	10
Mean (SD)	6.19 (26.18)
Week 24 (MMRM)	
n	10
LS mean (SE)	73.33 (5.42)
95% CI of LS mean	(60.40, 86.27)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	6.19 (5.42)
95% CI of LS mean	(-6.75, 19.13)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	6.67 (6.03)
95% CI of LS mean	(-7.28, 20.62)
P-value	0.3018

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	42
Mean (SD)	77.12 (21.75)
Week 4 (MMRM)	
n	42
LS mean (SE)	79.63 (2.39)
95% CI of LS mean	(74.80, 84.46)
Absolute Change at Week 4 (MMRM)	
n	42
LS mean (SE)	2.51 (2.39)
95% CI of LS mean	(-2.31, 7.34)
Week 8 (MMRM)	
n	42
LS mean (SE)	80.69 (2.50)
95% CI of LS mean	(75.64, 85.74)
Absolute Change at Week 8 (MMRM)	
n	42
LS mean (SE)	3.57 (2.50)
95% CI of LS mean	(-1.48, 8.62)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 12 (MMRM)	
n	41
LS mean (SE)	81.21 (3.04)
95% CI of LS mean	(75.07, 87.34)
Absolute Change at Week 12 (MMRM)	
n	41
LS mean (SE)	4.09 (3.04)
95% CI of LS mean	(-2.04, 10.22)
Week 16 (MMRM)	
n	42
LS mean (SE)	81.22 (3.33)
95% CI of LS mean	(74.49, 87.94)
Absolute Change at Week 16 (MMRM)	
n	42
LS mean (SE)	4.10 (3.33)
95% CI of LS mean	(-2.63, 10.83)
Week 24	
n	44
Mean (SD)	81.57 (22.34)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 24	
n	42
Mean (SD)	4.63 (22.02)
Week 24 (MMRM)	
n	44
LS mean (SE)	81.75 (3.15)
95% CI of LS mean	(75.37, 88.12)
Absolute Change at Week 24 (MMRM)	
n	42
LS mean (SE)	4.63 (3.15)
95% CI of LS mean	(-1.74, 11.00)
Absolute Change through Week 24 (MMRM)	
n	42
LS mean (SE)	4.37 (2.89)
95% CI of LS mean	(-1.48, 10.21)
P-value	0.1390

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	33
Mean (SD)	75.42 (20.74)
Week 4 (MMRM)	
n	33
LS mean (SE)	78.45 (3.39)
95% CI of LS mean	(71.51, 85.40)
Absolute Change at Week 4 (MMRM)	
n	33
LS mean (SE)	3.03 (3.39)
95% CI of LS mean	(-3.92, 9.98)
Week 8 (MMRM)	
n	33
LS mean (SE)	78.28 (2.82)
95% CI of LS mean	(72.52, 84.04)
Absolute Change at Week 8 (MMRM)	
n	33
LS mean (SE)	2.86 (2.82)
95% CI of LS mean	(-2.90, 8.62)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 12 (MMRM)	
n	33
LS mean (SE)	80.47 (2.11)
95% CI of LS mean	(76.16, 84.78)
Absolute Change at Week 12 (MMRM)	
n	33
LS mean (SE)	5.05 (2.11)
95% CI of LS mean	(0.74, 9.36)
Week 16 (MMRM)	
n	33
LS mean (SE)	77.44 (3.67)
95% CI of LS mean	(69.94, 84.94)
Absolute Change at Week 16 (MMRM)	
n	33
LS mean (SE)	2.02 (3.67)
95% CI of LS mean	(-5.48, 9.52)
Week 24	
n	34
Mean (SD)	82.03 (20.29)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 24	
n	33
Mean (SD)	6.40 (16.90)
Week 24 (MMRM)	
n	34
LS mean (SE)	81.82 (2.67)
95% CI of LS mean	(76.36, 87.28)
Absolute Change at Week 24 (MMRM)	
n	33
LS mean (SE)	6.40 (2.67)
95% CI of LS mean	(0.94, 11.86)
Absolute Change through Week 24 (MMRM)	
n	33
LS mean (SE)	4.21 (2.44)
95% CI of LS mean	(-0.77, 9.18)
P-value	0.0943

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	74.82 (21.48)
Week 4 (MMRM)	
n	47
LS mean (SE)	75.41 (2.56)
95% CI of LS mean	(70.26, 80.57)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	0.59 (2.56)
95% CI of LS mean	(-4.56, 5.74)
Week 8 (MMRM)	
n	47
LS mean (SE)	75.30 (2.40)
95% CI of LS mean	(70.47, 80.12)
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	0.47 (2.40)
95% CI of LS mean	(-4.35, 5.30)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 12 (MMRM)	
n	47
LS mean (SE)	78.01 (2.52)
95% CI of LS mean	(72.94, 83.08)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	3.19 (2.52)
95% CI of LS mean	(-1.88, 8.26)
Week 16 (MMRM)	
n	47
LS mean (SE)	78.49 (3.00)
95% CI of LS mean	(72.44, 84.54)
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	3.66 (3.00)
95% CI of LS mean	(-2.39, 9.72)
Week 24	
n	47
Mean (SD)	78.72 (23.95)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 24	
n	47
Mean (SD)	3.90 (18.93)
Week 24 (MMRM)	
n	47
LS mean (SE)	78.72 (2.66)
95% CI of LS mean	(73.38, 84.07)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	3.90 (2.66)
95% CI of LS mean	(-1.45, 9.25)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	3.78 (2.51)
95% CI of LS mean	(-1.28, 8.84)
P-value	0.1390

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	28
Mean (SD)	78.97 (20.81)
Week 4 (MMRM)	
n	28
LS mean (SE)	85.32 (2.52)
95% CI of LS mean	(80.11, 90.52)
Absolute Change at Week 4 (MMRM)	
n	28
LS mean (SE)	6.35 (2.52)
95% CI of LS mean	(1.15, 11.55)
Week 8 (MMRM)	
n	28
LS mean (SE)	86.90 (2.63)
95% CI of LS mean	(81.49, 92.32)
Absolute Change at Week 8 (MMRM)	
n	28
LS mean (SE)	7.94 (2.63)
95% CI of LS mean	(2.52, 13.35)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 12 (MMRM)	
n	27
LS mean (SE)	85.72 (2.73)
95% CI of LS mean	(80.11, 91.32)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	6.75 (2.73)
95% CI of LS mean	(1.15, 12.35)
Week 16 (MMRM)	
n	28
LS mean (SE)	81.35 (4.28)
95% CI of LS mean	(72.55, 90.15)
Absolute Change at Week 16 (MMRM)	
n	28
LS mean (SE)	2.38 (4.28)
95% CI of LS mean	(-6.42, 11.18)
Week 24	
n	31
Mean (SD)	86.38 (15.90)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 24	
n	28
Mean (SD)	7.94 (21.35)
Week 24 (MMRM)	
n	31
LS mean (SE)	86.90 (3.08)
95% CI of LS mean	(80.56, 93.25)
Absolute Change at Week 24 (MMRM)	
n	28
LS mean (SE)	7.94 (3.08)
95% CI of LS mean	(1.59, 14.29)
Absolute Change through Week 24 (MMRM)	
n	28
LS mean (SE)	5.16 (2.81)
95% CI of LS mean	(-0.64, 10.96)
P-value	0.0789

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	59
Mean (SD)	78.91 (20.50)
Week 4 (MMRM)	
n	59
LS mean (SE)	80.60 (2.05)
95% CI of LS mean	(76.51, 84.70)
Absolute Change at Week 4 (MMRM)	
n	59
LS mean (SE)	1.69 (2.05)
95% CI of LS mean	(-2.40, 5.79)
Week 8 (MMRM)	
n	59
LS mean (SE)	83.33 (1.99)
95% CI of LS mean	(79.35, 87.32)
Absolute Change at Week 8 (MMRM)	
n	59
LS mean (SE)	4.43 (1.99)
95% CI of LS mean	(0.44, 8.41)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 12 (MMRM)	
n	58
LS mean (SE)	83.41 (2.04)
95% CI of LS mean	(79.32, 87.50)
Absolute Change at Week 12 (MMRM)	
n	58
LS mean (SE)	4.50 (2.04)
95% CI of LS mean	(0.41, 8.59)
Week 16 (MMRM)	
n	59
LS mean (SE)	83.05 (2.49)
95% CI of LS mean	(78.06, 88.05)
Absolute Change at Week 16 (MMRM)	
n	59
LS mean (SE)	4.14 (2.49)
95% CI of LS mean	(-0.85, 9.14)
Week 24	
n	62
Mean (SD)	85.48 (17.26)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 24	
n	59
Mean (SD)	6.78 (17.99)
Week 24 (MMRM)	
n	62
LS mean (SE)	85.69 (1.90)
95% CI of LS mean	(81.88, 89.49)
Absolute Change at Week 24 (MMRM)	
n	59
LS mean (SE)	6.78 (1.90)
95% CI of LS mean	(2.98, 10.58)
Absolute Change through Week 24 (MMRM)	
n	59
LS mean (SE)	5.46 (1.89)
95% CI of LS mean	(1.69, 9.24)
P-value	0.0053

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	68.33 (22.23)
Week 4 (MMRM)	
n	10
LS mean (SE)	75.56 (4.24)
95% CI of LS mean	(65.92, 85.19)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	7.22 (4.24)
95% CI of LS mean	(-2.41, 16.86)
Week 8 (MMRM)	
n	10
LS mean (SE)	68.89 (3.81)
95% CI of LS mean	(60.14, 77.64)
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	0.56 (3.81)
95% CI of LS mean	(-8.20, 9.31)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 12 (MMRM)	
n	10
LS mean (SE)	77.78 (3.91)
95% CI of LS mean	(68.89, 86.67)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	9.44 (3.91)
95% CI of LS mean	(0.56, 18.33)
Week 16 (MMRM)	
n	10
LS mean (SE)	72.22 (4.56)
95% CI of LS mean	(61.74, 82.70)
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	3.89 (4.56)
95% CI of LS mean	(-6.59, 14.37)
Week 24	
n	10
Mean (SD)	73.33 (27.81)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 24	
n	10
Mean (SD)	5.00 (13.47)
Week 24 (MMRM)	
n	10
LS mean (SE)	73.33 (4.18)
95% CI of LS mean	(63.80, 82.86)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	5.00 (4.18)
95% CI of LS mean	(-4.53, 14.53)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	4.44 (3.36)
95% CI of LS mean	(-3.41, 12.30)
P-value	0.2251

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: Body (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.1284
Region (North America vs. Rest of the World)	0.6770
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.9477

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Body (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.5745
Region (North America vs. Rest of the World)	0.5410
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.1735

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Digestion (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.1053
Region (North America vs. Rest of the World)	0.6606
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.2280

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Eat (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.1374
Region (North America vs. Rest of the World)	0.8245
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.5137

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Emotion (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.3551
Region (North America vs. Rest of the World)	0.0852
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.8761

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Health Perceptions (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.1374
Region (North America vs. Rest of the World)	0.6299
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.9767

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Physical (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: School (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.9168
Region (North America vs. Rest of the World)	0.7182
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.2702

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R School (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.6739
Region (North America vs. Rest of the World)	0.5357
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.0712

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Treatment Burden (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.4364
Region (North America vs. Rest of the World)	0.7135
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.1369

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Vitality (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.9242
Region (North America vs. Rest of the World)	0.1453
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.4678

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Weight (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	80.81 (26.72)
Week 4 (MMRM)	
n	44
LS mean (SE)	84.60 (2.08)
95% CI of LS mean	(80.40, 88.79)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	3.79 (2.08)
95% CI of LS mean	(-0.41, 7.98)
Week 8 (MMRM)	
n	44
LS mean (SE)	81.82 (2.21)
95% CI of LS mean	(77.35, 86.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	1.01 (2.21)
95% CI of LS mean	(-3.46, 5.48)
Week 12 (MMRM)	
n	43
LS mean (SE)	84.80 (2.17)
95% CI of LS mean	(80.42, 89.17)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	3.99 (2.17)
95% CI of LS mean	(-0.38, 8.36)
Week 16 (MMRM)	
n	44
LS mean (SE)	87.88 (2.64)
95% CI of LS mean	(82.54, 93.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	7.07 (2.64)
95% CI of LS mean	(1.73, 12.41)
Week 24	
n	44
Mean (SD)	87.37 (21.24)
Absolute Change at Week 24	
n	44
Mean (SD)	6.57 (15.22)
Week 24 (MMRM)	
n	44
LS mean (SE)	87.37 (1.85)
95% CI of LS mean	(83.64, 91.11)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	6.57 (1.85)
95% CI of LS mean	(2.83, 10.30)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	6.82 (2.04)
95% CI of LS mean	(2.68, 10.96)
P-value	0.0019

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	79.25 (25.63)
Week 4 (MMRM)	
n	34
LS mean (SE)	77.12 (2.69)
95% CI of LS mean	(71.60, 82.65)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	-2.12 (2.69)
95% CI of LS mean	(-7.65, 3.40)
Week 8 (MMRM)	
n	34
LS mean (SE)	83.33 (3.06)
95% CI of LS mean	(77.05, 89.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	4.08 (3.06)
95% CI of LS mean	(-2.20, 10.37)
Week 12 (MMRM)	
n	34
LS mean (SE)	83.33 (2.89)
95% CI of LS mean	(77.43, 89.24)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	4.08 (2.89)
95% CI of LS mean	(-1.82, 9.99)
Week 16 (MMRM)	
n	34
LS mean (SE)	83.33 (2.61)
95% CI of LS mean	(78.01, 88.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	4.08 (2.61)
95% CI of LS mean	(-1.24, 9.41)
Week 24	
n	34
Mean (SD)	78.76 (20.90)
Absolute Change at Week 24	
n	34
Mean (SD)	-0.49 (19.93)
Week 24 (MMRM)	
n	34
LS mean (SE)	78.76 (2.80)
95% CI of LS mean	(73.05, 84.47)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	-0.49 (2.80)
95% CI of LS mean	(-6.20, 5.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	1.80 (2.32)
95% CI of LS mean	(-2.95, 6.54)
P-value	0.4451

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	80.14 (25.05)
Week 4 (MMRM)	
n	47
LS mean (SE)	82.03 (2.24)
95% CI of LS mean	(77.51, 86.56)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	1.89 (2.24)
95% CI of LS mean	(-2.63, 6.41)
Week 8 (MMRM)	
n	47
LS mean (SE)	82.03 (1.89)
95% CI of LS mean	(78.23, 85.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	1.89 (1.89)
95% CI of LS mean	(-1.91, 5.70)
Week 12 (MMRM)	
n	47
LS mean (SE)	83.22 (2.35)
95% CI of LS mean	(78.48, 87.95)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	3.07 (2.35)
95% CI of LS mean	(-1.67, 7.81)
Week 16 (MMRM)	
n	47
LS mean (SE)	87.47 (2.69)
95% CI of LS mean	(82.04, 92.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	7.33 (2.69)
95% CI of LS mean	(1.90, 12.75)
Week 24	
n	47
Mean (SD)	82.51 (21.20)
Absolute Change at Week 24	
n	47
Mean (SD)	2.36 (18.53)
Week 24 (MMRM)	
n	47
LS mean (SE)	82.51 (2.25)
95% CI of LS mean	(77.97, 87.04)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	2.36 (2.25)
95% CI of LS mean	(-2.17, 6.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	4.85 (2.24)
95% CI of LS mean	(0.33, 9.36)
P-value	0.0361

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	80.11 (28.03)
Week 4 (MMRM)	
n	31
LS mean (SE)	80.29 (2.31)
95% CI of LS mean	(75.56, 85.01)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	0.18 (2.31)
95% CI of LS mean	(-4.54, 4.90)
Week 8 (MMRM)	
n	31
LS mean (SE)	83.15 (3.82)
95% CI of LS mean	(75.33, 90.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	3.05 (3.82)
95% CI of LS mean	(-4.78, 10.87)
Week 12 (MMRM)	
n	30
LS mean (SE)	85.67 (2.72)
95% CI of LS mean	(80.09, 91.24)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	5.56 (2.72)
95% CI of LS mean	(-0.02, 11.14)
Week 16 (MMRM)	
n	31
LS mean (SE)	83.51 (2.42)
95% CI of LS mean	(78.54, 88.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	3.41 (2.42)
95% CI of LS mean	(-1.57, 8.38)
Week 24	
n	31
Mean (SD)	85.30 (21.92)
Absolute Change at Week 24	
n	31
Mean (SD)	5.20 (16.41)
Week 24 (MMRM)	
n	31
LS mean (SE)	85.30 (2.48)
95% CI of LS mean	(80.21, 90.40)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	5.20 (2.48)
95% CI of LS mean	(0.10, 10.30)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	4.30 (2.10)
95% CI of LS mean	(-0.03, 8.63)
P-value	0.0516

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	76.97 (27.84)
Week 4 (MMRM)	
n	62
LS mean (SE)	78.85 (1.96)
95% CI of LS mean	(74.94, 82.77)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	1.88 (1.96)
95% CI of LS mean	(-2.04, 5.80)
Week 8 (MMRM)	
n	62
LS mean (SE)	81.54 (1.94)
95% CI of LS mean	(77.66, 85.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	4.57 (1.94)
95% CI of LS mean	(0.69, 8.45)
Week 12 (MMRM)	
n	61
LS mean (SE)	82.59 (1.97)
95% CI of LS mean	(78.66, 86.52)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	5.62 (1.97)
95% CI of LS mean	(1.68, 9.55)
Week 16 (MMRM)	
n	62
LS mean (SE)	84.95 (1.98)
95% CI of LS mean	(80.99, 88.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	7.97 (1.98)
95% CI of LS mean	(4.02, 11.93)
Week 24	
n	62
Mean (SD)	81.54 (22.22)
Absolute Change at Week 24	
n	62
Mean (SD)	4.57 (19.02)
Week 24 (MMRM)	
n	62
LS mean (SE)	81.54 (1.98)
95% CI of LS mean	(77.58, 85.50)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	4.57 (1.98)
95% CI of LS mean	(0.61, 8.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	6.27 (1.76)
95% CI of LS mean	(2.75, 9.79)
P-value	0.0007

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	91.11 (14.63)
Week 4 (MMRM)	
n	10
LS mean (SE)	91.11 (4.12)
95% CI of LS mean	(82.76, 99.46)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	0.00 (4.12)
95% CI of LS mean	(-8.35, 8.35)
Week 8 (MMRM)	
n	10
LS mean (SE)	84.44 (4.12)
95% CI of LS mean	(76.09, 92.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	-6.67 (4.12)
95% CI of LS mean	(-15.02, 1.69)
Week 12 (MMRM)	
n	10
LS mean (SE)	88.89 (4.12)
95% CI of LS mean	(80.54, 97.24)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	-2.22 (4.12)
95% CI of LS mean	(-10.57, 6.13)
Week 16 (MMRM)	
n	10
LS mean (SE)	84.44 (4.12)
95% CI of LS mean	(76.09, 92.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	-6.67 (4.12)
95% CI of LS mean	(-15.02, 1.69)
Week 24	
n	10
Mean (SD)	88.89 (18.89)
Absolute Change at Week 24	
n	10
Mean (SD)	-2.22 (8.76)
Week 24 (MMRM)	
n	10
LS mean (SE)	88.89 (4.12)
95% CI of LS mean	(80.54, 97.24)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	-2.22 (4.12)
95% CI of LS mean	(-10.57, 6.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	-4.44 (3.13)
95% CI of LS mean	(-10.97, 2.08)
P-value	0.1706

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	80.81 (17.67)
Week 4 (MMRM)	
n	44
LS mean (SE)	80.05 (2.66)
95% CI of LS mean	(74.69, 85.41)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	-0.76 (2.66)
95% CI of LS mean	(-6.12, 4.60)
Week 8 (MMRM)	
n	44
LS mean (SE)	83.33 (2.05)
95% CI of LS mean	(79.19, 87.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	2.53 (2.05)
95% CI of LS mean	(-1.62, 6.67)
Week 12 (MMRM)	
n	43
LS mean (SE)	83.65 (2.12)
95% CI of LS mean	(79.38, 87.92)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	2.85 (2.12)
95% CI of LS mean	(-1.43, 7.12)
Week 16 (MMRM)	
n	44
LS mean (SE)	86.11 (1.65)
95% CI of LS mean	(82.78, 89.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	5.30 (1.65)
95% CI of LS mean	(1.97, 8.64)
Week 24	
n	44
Mean (SD)	82.58 (16.84)
Absolute Change at Week 24	
n	44
Mean (SD)	1.77 (15.52)
Week 24 (MMRM)	
n	44
LS mean (SE)	82.58 (2.08)
95% CI of LS mean	(78.38, 86.78)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	1.77 (2.08)
95% CI of LS mean	(-2.43, 5.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	3.54 (1.64)
95% CI of LS mean	(0.23, 6.85)
P-value	0.0369

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	83.99 (17.12)
Week 4 (MMRM)	
n	34
LS mean (SE)	86.60 (1.90)
95% CI of LS mean	(82.73, 90.47)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	2.61 (1.90)
95% CI of LS mean	(-1.25, 6.48)
Week 8 (MMRM)	
n	34
LS mean (SE)	81.70 (2.56)
95% CI of LS mean	(76.48, 86.92)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	-2.29 (2.56)
95% CI of LS mean	(-7.50, 2.93)
Week 12 (MMRM)	
n	34
LS mean (SE)	84.31 (2.15)
95% CI of LS mean	(79.92, 88.70)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	0.33 (2.15)
95% CI of LS mean	(-4.06, 4.72)
Week 16 (MMRM)	
n	34
LS mean (SE)	84.64 (2.08)
95% CI of LS mean	(80.41, 88.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	0.65 (2.08)
95% CI of LS mean	(-3.58, 4.88)
Week 24	
n	34
Mean (SD)	80.07 (16.13)
Absolute Change at Week 24	
n	34
Mean (SD)	-3.92 (17.06)
Week 24 (MMRM)	
n	34
LS mean (SE)	80.07 (2.45)
95% CI of LS mean	(75.07, 85.06)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	-3.92 (2.45)
95% CI of LS mean	(-8.92, 1.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	-1.63 (1.94)
95% CI of LS mean	(-5.60, 2.33)
P-value	0.4071

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	80.85 (18.78)
Week 4 (MMRM)	
n	47
LS mean (SE)	83.69 (1.78)
95% CI of LS mean	(80.10, 87.27)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	2.84 (1.78)
95% CI of LS mean	(-0.75, 6.42)
Week 8 (MMRM)	
n	47
LS mean (SE)	81.56 (2.18)
95% CI of LS mean	(77.17, 85.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	0.71 (2.18)
95% CI of LS mean	(-3.68, 5.10)
Week 12 (MMRM)	
n	47
LS mean (SE)	82.74 (1.91)
95% CI of LS mean	(78.90, 86.59)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	1.89 (1.91)
95% CI of LS mean	(-1.95, 5.74)
Week 16 (MMRM)	
n	47
LS mean (SE)	85.34 (1.64)
95% CI of LS mean	(82.04, 88.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	4.49 (1.64)
95% CI of LS mean	(1.19, 7.79)
Week 24	
n	47
Mean (SD)	81.56 (14.33)
Absolute Change at Week 24	
n	47
Mean (SD)	0.71 (16.45)
Week 24 (MMRM)	
n	47
LS mean (SE)	81.56 (1.83)
95% CI of LS mean	(77.88, 85.24)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	0.71 (1.83)
95% CI of LS mean	(-2.98, 4.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	2.60 (1.52)
95% CI of LS mean	(-0.47, 5.67)
P-value	0.0949

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	84.23 (15.12)
Week 4 (MMRM)	
n	31
LS mean (SE)	81.72 (3.37)
95% CI of LS mean	(74.83, 88.61)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	-2.51 (3.37)
95% CI of LS mean	(-9.40, 4.38)
Week 8 (MMRM)	
n	31
LS mean (SE)	84.23 (2.41)
95% CI of LS mean	(79.30, 89.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	0.00 (2.41)
95% CI of LS mean	(-4.93, 4.93)
Week 12 (MMRM)	
n	30
LS mean (SE)	86.08 (2.58)
95% CI of LS mean	(80.77, 91.39)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	1.85 (2.58)
95% CI of LS mean	(-3.46, 7.16)
Week 16 (MMRM)	
n	31
LS mean (SE)	85.66 (2.12)
95% CI of LS mean	(81.32, 90.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	1.43 (2.12)
95% CI of LS mean	(-2.91, 5.77)
Week 24	
n	31
Mean (SD)	81.36 (19.54)
Absolute Change at Week 24	
n	31
Mean (SD)	-2.87 (16.22)
Week 24 (MMRM)	
n	31
LS mean (SE)	81.36 (3.13)
95% CI of LS mean	(74.93, 87.79)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	-2.87 (3.13)
95% CI of LS mean	(-9.29, 3.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	-0.72 (2.32)
95% CI of LS mean	(-5.49, 4.05)
P-value	0.7595

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	80.11 (17.56)
Week 4 (MMRM)	
n	62
LS mean (SE)	82.26 (1.85)
95% CI of LS mean	(78.55, 85.96)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	2.15 (1.85)
95% CI of LS mean	(-1.55, 5.86)
Week 8 (MMRM)	
n	62
LS mean (SE)	80.82 (1.90)
95% CI of LS mean	(77.03, 84.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	0.72 (1.90)
95% CI of LS mean	(-3.08, 4.51)
Week 12 (MMRM)	
n	61
LS mean (SE)	82.60 (1.83)
95% CI of LS mean	(78.95, 86.26)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	2.49 (1.83)
95% CI of LS mean	(-1.16, 6.15)
Week 16 (MMRM)	
n	62
LS mean (SE)	83.51 (1.54)
95% CI of LS mean	(80.43, 86.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	3.41 (1.54)
95% CI of LS mean	(0.33, 6.48)
Week 24	
n	62
Mean (SD)	78.85 (16.43)
Absolute Change at Week 24	
n	62
Mean (SD)	-1.25 (17.78)
Week 24 (MMRM)	
n	62
LS mean (SE)	78.85 (1.87)
95% CI of LS mean	(75.12, 82.58)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	-1.25 (1.87)
95% CI of LS mean	(-4.99, 2.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	1.08 (1.48)
95% CI of LS mean	(-1.88, 4.03)
P-value	0.4694

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	90.00 (17.72)
Week 4 (MMRM)	
n	10
LS mean (SE)	82.22 (7.20)
95% CI of LS mean	(65.83, 98.62)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	-7.78 (7.20)
95% CI of LS mean	(-24.17, 8.62)
Week 8 (MMRM)	
n	10
LS mean (SE)	91.11 (4.14)
95% CI of LS mean	(81.62, 100.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	1.11 (4.14)
95% CI of LS mean	(-8.38, 10.60)
Week 12 (MMRM)	
n	10
LS mean (SE)	91.11 (2.50)
95% CI of LS mean	(85.38, 96.84)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	1.11 (2.50)
95% CI of LS mean	(-4.62, 6.84)
Week 16 (MMRM)	
n	10
LS mean (SE)	93.33 (2.31)
95% CI of LS mean	(87.83, 98.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	3.33 (2.31)
95% CI of LS mean	(-2.17, 8.84)
Week 24	
n	10
Mean (SD)	93.33 (11.94)
Absolute Change at Week 24	
n	10
Mean (SD)	3.33 (9.15)
Week 24 (MMRM)	
n	10
LS mean (SE)	93.33 (1.83)
95% CI of LS mean	(88.80, 97.87)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	3.33 (1.83)
95% CI of LS mean	(-1.20, 7.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	3.33 (1.27)
95% CI of LS mean	(0.29, 6.37)
P-value	0.0361

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	81.06 (25.31)
Week 4 (MMRM)	
n	44
LS mean (SE)	82.20 (2.29)
95% CI of LS mean	(77.57, 86.82)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	1.14 (2.29)
95% CI of LS mean	(-3.49, 5.76)
Week 8 (MMRM)	
n	44
LS mean (SE)	82.20 (2.88)
95% CI of LS mean	(76.38, 88.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	1.14 (2.88)
95% CI of LS mean	(-4.68, 6.95)
Week 12 (MMRM)	
n	43
LS mean (SE)	82.99 (2.63)
95% CI of LS mean	(77.67, 88.31)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	1.93 (2.63)
95% CI of LS mean	(-3.39, 7.25)
Week 16 (MMRM)	
n	44
LS mean (SE)	83.71 (2.11)
95% CI of LS mean	(79.45, 87.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	2.65 (2.11)
95% CI of LS mean	(-1.61, 6.91)
Week 24	
n	44
Mean (SD)	84.47 (21.98)
Absolute Change at Week 24	
n	44
Mean (SD)	3.41 (17.82)
Week 24 (MMRM)	
n	44
LS mean (SE)	84.47 (2.31)
95% CI of LS mean	(79.80, 89.14)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	3.41 (2.31)
95% CI of LS mean	(-1.26, 8.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	3.03 (1.85)
95% CI of LS mean	(-0.71, 6.77)
P-value	0.1096

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	77.45 (26.23)
Week 4 (MMRM)	
n	34
LS mean (SE)	73.53 (3.09)
95% CI of LS mean	(67.24, 79.82)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	-3.92 (3.09)
95% CI of LS mean	(-10.22, 2.37)
Week 8 (MMRM)	
n	34
LS mean (SE)	75.49 (3.11)
95% CI of LS mean	(69.15, 81.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	-1.96 (3.11)
95% CI of LS mean	(-8.30, 4.38)
Week 12 (MMRM)	
n	34
LS mean (SE)	72.06 (3.27)
95% CI of LS mean	(65.41, 78.71)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	-5.39 (3.27)
95% CI of LS mean	(-12.05, 1.26)
Week 16 (MMRM)	
n	34
LS mean (SE)	77.45 (2.66)
95% CI of LS mean	(72.02, 82.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	0.00 (2.66)
95% CI of LS mean	(-5.43, 5.43)
Week 24	
n	34
Mean (SD)	78.43 (26.44)
Absolute Change at Week 24	
n	34
Mean (SD)	0.98 (19.65)
Week 24 (MMRM)	
n	34
LS mean (SE)	78.43 (3.20)
95% CI of LS mean	(71.91, 84.95)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	0.98 (3.20)
95% CI of LS mean	(-5.54, 7.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	0.49 (2.70)
95% CI of LS mean	(-5.02, 6.00)
P-value	0.8573

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	75.89 (27.54)
Week 4 (MMRM)	
n	47
LS mean (SE)	76.24 (2.53)
95% CI of LS mean	(71.15, 81.33)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	0.35 (2.53)
95% CI of LS mean	(-4.73, 5.44)
Week 8 (MMRM)	
n	47
LS mean (SE)	77.66 (2.59)
95% CI of LS mean	(72.45, 82.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	1.77 (2.59)
95% CI of LS mean	(-3.44, 6.99)
Week 12 (MMRM)	
n	47
LS mean (SE)	75.53 (2.47)
95% CI of LS mean	(70.54, 80.52)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	-0.35 (2.47)
95% CI of LS mean	(-5.35, 4.64)
Week 16 (MMRM)	
n	47
LS mean (SE)	79.08 (2.16)
95% CI of LS mean	(74.71, 83.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	3.19 (2.16)
95% CI of LS mean	(-1.17, 7.56)
Week 24	
n	47
Mean (SD)	80.85 (25.06)
Absolute Change at Week 24	
n	47
Mean (SD)	4.96 (19.01)
Week 24 (MMRM)	
n	47
LS mean (SE)	80.85 (2.49)
95% CI of LS mean	(75.83, 85.87)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	4.96 (2.49)
95% CI of LS mean	(-0.06, 9.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	4.08 (2.13)
95% CI of LS mean	(-0.21, 8.37)
P-value	0.0620

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	84.95 (21.67)
Week 4 (MMRM)	
n	31
LS mean (SE)	81.72 (2.80)
95% CI of LS mean	(76.00, 87.44)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	-3.23 (2.80)
95% CI of LS mean	(-8.94, 2.49)
Week 8 (MMRM)	
n	31
LS mean (SE)	81.72 (3.54)
95% CI of LS mean	(74.48, 88.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	-3.23 (3.54)
95% CI of LS mean	(-10.47, 4.02)
Week 12 (MMRM)	
n	30
LS mean (SE)	82.58 (3.67)
95% CI of LS mean	(75.07, 90.10)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	-2.36 (3.67)
95% CI of LS mean	(-9.88, 5.15)
Week 16 (MMRM)	
n	31
LS mean (SE)	83.87 (2.68)
95% CI of LS mean	(78.38, 89.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	-1.08 (2.68)
95% CI of LS mean	(-6.56, 4.41)
Week 24	
n	31
Mean (SD)	83.33 (22.77)
Absolute Change at Week 24	
n	31
Mean (SD)	-1.61 (17.40)
Week 24 (MMRM)	
n	31
LS mean (SE)	83.33 (2.96)
95% CI of LS mean	(77.29, 89.38)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	-1.61 (2.96)
95% CI of LS mean	(-7.66, 4.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	-1.34 (2.35)
95% CI of LS mean	(-6.15, 3.46)
P-value	0.5713

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	78.49 (26.89)
Week 4 (MMRM)	
n	62
LS mean (SE)	76.88 (2.29)
95% CI of LS mean	(72.30, 81.47)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	-1.61 (2.29)
95% CI of LS mean	(-6.20, 2.97)
Week 8 (MMRM)	
n	62
LS mean (SE)	78.23 (2.53)
95% CI of LS mean	(73.16, 83.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	-0.27 (2.53)
95% CI of LS mean	(-5.34, 4.80)
Week 12 (MMRM)	
n	61
LS mean (SE)	76.31 (2.51)
95% CI of LS mean	(71.29, 81.33)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	-2.19 (2.51)
95% CI of LS mean	(-7.21, 2.83)
Week 16 (MMRM)	
n	62
LS mean (SE)	79.84 (1.91)
95% CI of LS mean	(76.02, 83.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	1.34 (1.91)
95% CI of LS mean	(-2.48, 5.16)
Week 24	
n	62
Mean (SD)	79.84 (25.27)
Absolute Change at Week 24	
n	62
Mean (SD)	1.34 (19.86)
Week 24 (MMRM)	
n	62
LS mean (SE)	79.84 (2.26)
95% CI of LS mean	(75.31, 84.37)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	1.34 (2.26)
95% CI of LS mean	(-3.18, 5.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	1.34 (1.83)
95% CI of LS mean	(-2.32, 5.01)
P-value	0.4661

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	91.67 (14.16)
Week 4 (MMRM)	
n	10
LS mean (SE)	90.00 (2.01)
95% CI of LS mean	(85.93, 94.07)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	-1.67 (2.01)
95% CI of LS mean	(-5.74, 2.40)
Week 8 (MMRM)	
n	10
LS mean (SE)	90.00 (2.01)
95% CI of LS mean	(85.93, 94.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	-1.67 (2.01)
95% CI of LS mean	(-5.74, 2.40)
Week 12 (MMRM)	
n	10
LS mean (SE)	91.67 (2.01)
95% CI of LS mean	(87.60, 95.74)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	0.00 (2.01)
95% CI of LS mean	(-4.07, 4.07)
Week 16 (MMRM)	
n	10
LS mean (SE)	93.33 (2.01)
95% CI of LS mean	(89.26, 97.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	1.67 (2.01)
95% CI of LS mean	(-2.40, 5.74)
Week 24	
n	10
Mean (SD)	96.67 (7.03)
Absolute Change at Week 24	
n	10
Mean (SD)	5.00 (8.05)
Week 24 (MMRM)	
n	10
LS mean (SE)	96.67 (2.01)
95% CI of LS mean	(92.60, 100.74)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	5.00 (2.01)
95% CI of LS mean	(0.93, 9.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	3.33 (1.24)
95% CI of LS mean	(0.83, 5.84)
P-value	0.0105

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	86.82 (12.41)
Week 4 (MMRM)	
n	44
LS mean (SE)	88.48 (1.29)
95% CI of LS mean	(85.87, 91.10)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	1.67 (1.29)
95% CI of LS mean	(-0.95, 4.28)
Week 8 (MMRM)	
n	44
LS mean (SE)	87.58 (1.50)
95% CI of LS mean	(84.55, 90.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	0.76 (1.50)
95% CI of LS mean	(-2.27, 3.78)
Week 12 (MMRM)	
n	43
LS mean (SE)	89.92 (1.37)
95% CI of LS mean	(87.15, 92.68)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	3.10 (1.37)
95% CI of LS mean	(0.33, 5.86)
Week 16 (MMRM)	
n	44
LS mean (SE)	90.45 (1.56)
95% CI of LS mean	(87.32, 93.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	3.64 (1.56)
95% CI of LS mean	(0.50, 6.77)
Week 24	
n	44
Mean (SD)	89.85 (9.48)
Absolute Change at Week 24	
n	44
Mean (SD)	3.03 (11.72)
Week 24 (MMRM)	
n	44
LS mean (SE)	89.85 (1.32)
95% CI of LS mean	(87.18, 92.52)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	3.03 (1.32)
95% CI of LS mean	(0.36, 5.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	3.33 (1.04)
95% CI of LS mean	(1.23, 5.44)
P-value	0.0027

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	86.13 (13.63)
Week 4 (MMRM)	
n	34
LS mean (SE)	85.10 (1.83)
95% CI of LS mean	(81.37, 88.83)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	-1.03 (1.83)
95% CI of LS mean	(-4.76, 2.70)
Week 8 (MMRM)	
n	34
LS mean (SE)	85.59 (1.25)
95% CI of LS mean	(83.04, 88.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	-0.54 (1.25)
95% CI of LS mean	(-3.09, 2.01)
Week 12 (MMRM)	
n	34
LS mean (SE)	88.63 (1.57)
95% CI of LS mean	(85.43, 91.83)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	2.50 (1.57)
95% CI of LS mean	(-0.70, 5.70)
Week 16 (MMRM)	
n	34
LS mean (SE)	88.24 (1.42)
95% CI of LS mean	(85.34, 91.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	2.11 (1.42)
95% CI of LS mean	(-0.79, 5.00)
Week 24	
n	34
Mean (SD)	86.47 (12.66)
Absolute Change at Week 24	
n	34
Mean (SD)	0.34 (12.68)
Week 24 (MMRM)	
n	34
LS mean (SE)	86.47 (1.86)
95% CI of LS mean	(82.68, 90.26)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	0.34 (1.86)
95% CI of LS mean	(-3.45, 4.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	1.23 (1.35)
95% CI of LS mean	(-1.55, 4.00)
P-value	0.3727

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	86.84 (13.76)
Week 4 (MMRM)	
n	47
LS mean (SE)	87.52 (1.37)
95% CI of LS mean	(84.75, 90.28)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	0.67 (1.37)
95% CI of LS mean	(-2.09, 3.44)
Week 8 (MMRM)	
n	47
LS mean (SE)	86.88 (1.19)
95% CI of LS mean	(84.48, 89.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	0.04 (1.19)
95% CI of LS mean	(-2.37, 2.44)
Week 12 (MMRM)	
n	47
LS mean (SE)	89.08 (1.32)
95% CI of LS mean	(86.42, 91.73)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	2.23 (1.32)
95% CI of LS mean	(-0.42, 4.89)
Week 16 (MMRM)	
n	47
LS mean (SE)	90.78 (1.19)
95% CI of LS mean	(88.39, 93.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	3.94 (1.19)
95% CI of LS mean	(1.55, 6.33)
Week 24	
n	47
Mean (SD)	88.51 (10.65)
Absolute Change at Week 24	
n	47
Mean (SD)	1.67 (10.97)
Week 24 (MMRM)	
n	47
LS mean (SE)	88.51 (1.24)
95% CI of LS mean	(86.00, 91.02)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	1.67 (1.24)
95% CI of LS mean	(-0.84, 4.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	2.80 (1.02)
95% CI of LS mean	(0.75, 4.85)
P-value	0.0085

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	86.02 (11.59)
Week 4 (MMRM)	
n	31
LS mean (SE)	86.24 (1.80)
95% CI of LS mean	(82.55, 89.92)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	0.22 (1.80)
95% CI of LS mean	(-3.47, 3.90)
Week 8 (MMRM)	
n	31
LS mean (SE)	86.45 (1.81)
95% CI of LS mean	(82.74, 90.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	0.43 (1.81)
95% CI of LS mean	(-3.29, 4.15)
Week 12 (MMRM)	
n	30
LS mean (SE)	89.96 (1.73)
95% CI of LS mean	(86.41, 93.51)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	3.94 (1.73)
95% CI of LS mean	(0.38, 7.49)
Week 16 (MMRM)	
n	31
LS mean (SE)	87.53 (1.94)
95% CI of LS mean	(83.55, 91.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	1.51 (1.94)
95% CI of LS mean	(-2.47, 5.49)
Week 24	
n	31
Mean (SD)	88.17 (11.76)
Absolute Change at Week 24	
n	31
Mean (SD)	2.15 (13.92)
Week 24 (MMRM)	
n	31
LS mean (SE)	88.17 (2.15)
95% CI of LS mean	(83.76, 92.58)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	2.15 (2.15)
95% CI of LS mean	(-2.26, 6.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	1.83 (1.47)
95% CI of LS mean	(-1.18, 4.83)
P-value	0.2231

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	85.30 (13.80)
Week 4 (MMRM)	
n	62
LS mean (SE)	85.70 (1.13)
95% CI of LS mean	(83.45, 87.95)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	0.40 (1.13)
95% CI of LS mean	(-1.85, 2.66)
Week 8 (MMRM)	
n	62
LS mean (SE)	86.08 (1.07)
95% CI of LS mean	(83.94, 88.21)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	0.78 (1.07)
95% CI of LS mean	(-1.35, 2.91)
Week 12 (MMRM)	
n	61
LS mean (SE)	88.21 (1.14)
95% CI of LS mean	(85.93, 90.48)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	2.91 (1.14)
95% CI of LS mean	(0.63, 5.19)
Week 16 (MMRM)	
n	62
LS mean (SE)	88.60 (1.11)
95% CI of LS mean	(86.37, 90.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	3.31 (1.11)
95% CI of LS mean	(1.08, 5.54)
Week 24	
n	62
Mean (SD)	87.31 (11.50)
Absolute Change at Week 24	
n	62
Mean (SD)	2.02 (13.19)
Week 24 (MMRM)	
n	62
LS mean (SE)	87.31 (1.29)
95% CI of LS mean	(84.72, 89.90)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	2.02 (1.29)
95% CI of LS mean	(-0.57, 4.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	2.66 (0.91)
95% CI of LS mean	(0.84, 4.49)
P-value	0.0050

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	91.33 (7.06)
Week 4 (MMRM)	
n	10
LS mean (SE)	92.00 (5.43)
95% CI of LS mean	(76.64, 107.36)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	0.67 (5.43)
95% CI of LS mean	(-14.69, 16.03)
Week 8 (MMRM)	
n	10
LS mean (SE)	88.00 (4.64)
95% CI of LS mean	(71.39, 104.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	-3.33 (4.64)
95% CI of LS mean	(-19.95, 13.28)
Week 12 (MMRM)	
n	10
LS mean (SE)	92.67 (3.88)
95% CI of LS mean	(80.30, 105.03)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	1.33 (3.88)
95% CI of LS mean	(-11.03, 13.70)
Week 16 (MMRM)	
n	10
LS mean (SE)	92.00 (4.51)
95% CI of LS mean	(77.83, 106.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	0.67 (4.51)
95% CI of LS mean	(-13.51, 14.84)
Week 24	
n	10
Mean (SD)	92.67 (9.14)
Absolute Change at Week 24	
n	10
Mean (SD)	1.33 (5.26)
Week 24 (MMRM)	
n	10
LS mean (SE)	92.67 (1.97)
95% CI of LS mean	(83.18, 102.15)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	1.33 (1.97)
95% CI of LS mean	(-8.15, 10.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	1.00 (2.61)
95% CI of LS mean	(-24.19, 26.19)
P-value	0.7611

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	86.36 (14.94)
Week 4 (MMRM)	
n	44
LS mean (SE)	82.83 (2.33)
95% CI of LS mean	(78.11, 87.54)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	-3.54 (2.33)
95% CI of LS mean	(-8.25, 1.18)
Week 8 (MMRM)	
n	44
LS mean (SE)	83.84 (2.11)
95% CI of LS mean	(79.59, 88.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	-2.53 (2.11)
95% CI of LS mean	(-6.78, 1.73)
Week 12 (MMRM)	
n	43
LS mean (SE)	87.30 (1.51)
95% CI of LS mean	(84.25, 90.36)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	0.94 (1.51)
95% CI of LS mean	(-2.12, 3.99)
Week 16 (MMRM)	
n	44
LS mean (SE)	89.14 (1.69)
95% CI of LS mean	(85.74, 92.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	2.78 (1.69)
95% CI of LS mean	(-0.62, 6.18)
Week 24	
n	44
Mean (SD)	89.65 (14.85)
Absolute Change at Week 24	
n	44
Mean (SD)	3.28 (14.29)
Week 24 (MMRM)	
n	44
LS mean (SE)	89.65 (1.90)
95% CI of LS mean	(85.81, 93.48)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	3.28 (1.90)
95% CI of LS mean	(-0.55, 7.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	3.03 (1.34)
95% CI of LS mean	(0.32, 5.74)
P-value	0.0291

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	87.25 (12.27)
Week 4 (MMRM)	
n	34
LS mean (SE)	82.03 (2.17)
95% CI of LS mean	(77.61, 86.44)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	-5.23 (2.17)
95% CI of LS mean	(-9.65, -0.81)
Week 8 (MMRM)	
n	34
LS mean (SE)	88.56 (1.60)
95% CI of LS mean	(85.31, 91.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	1.31 (1.60)
95% CI of LS mean	(-1.95, 4.56)
Week 12 (MMRM)	
n	34
LS mean (SE)	86.27 (2.36)
95% CI of LS mean	(81.46, 91.09)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	-0.98 (2.36)
95% CI of LS mean	(-5.79, 3.83)
Week 16 (MMRM)	
n	34
LS mean (SE)	87.58 (1.68)
95% CI of LS mean	(84.16, 91.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	0.33 (1.68)
95% CI of LS mean	(-3.10, 3.75)
Week 24	
n	34
Mean (SD)	84.64 (18.56)
Absolute Change at Week 24	
n	34
Mean (SD)	-2.61 (18.56)
Week 24 (MMRM)	
n	34
LS mean (SE)	84.64 (3.08)
95% CI of LS mean	(78.36, 90.92)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	-2.61 (3.08)
95% CI of LS mean	(-8.89, 3.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	-1.14 (1.94)
95% CI of LS mean	(-5.11, 2.82)
P-value	0.5606

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	87.23 (12.69)
Week 4 (MMRM)	
n	47
LS mean (SE)	82.74 (1.91)
95% CI of LS mean	(78.88, 86.60)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	-4.49 (1.91)
95% CI of LS mean	(-8.35, -0.63)
Week 8 (MMRM)	
n	47
LS mean (SE)	86.76 (1.58)
95% CI of LS mean	(83.58, 89.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	-0.47 (1.58)
95% CI of LS mean	(-3.65, 2.71)
Week 12 (MMRM)	
n	47
LS mean (SE)	87.94 (1.77)
95% CI of LS mean	(84.38, 91.50)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	0.71 (1.77)
95% CI of LS mean	(-2.85, 4.27)
Week 16 (MMRM)	
n	47
LS mean (SE)	91.25 (1.33)
95% CI of LS mean	(88.57, 93.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	4.02 (1.33)
95% CI of LS mean	(1.33, 6.71)
Week 24	
n	47
Mean (SD)	89.60 (15.09)
Absolute Change at Week 24	
n	47
Mean (SD)	2.36 (13.89)
Week 24 (MMRM)	
n	47
LS mean (SE)	89.60 (1.89)
95% CI of LS mean	(85.80, 93.39)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	2.36 (1.89)
95% CI of LS mean	(-1.43, 6.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	3.19 (1.29)
95% CI of LS mean	(0.59, 5.79)
P-value	0.0173

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	86.02 (15.44)
Week 4 (MMRM)	
n	31
LS mean (SE)	82.08 (2.86)
95% CI of LS mean	(76.24, 87.92)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	-3.94 (2.86)
95% CI of LS mean	(-9.78, 1.90)
Week 8 (MMRM)	
n	31
LS mean (SE)	84.59 (2.50)
95% CI of LS mean	(79.46, 89.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	-1.43 (2.50)
95% CI of LS mean	(-6.56, 3.69)
Week 12 (MMRM)	
n	30
LS mean (SE)	85.23 (2.09)
95% CI of LS mean	(80.96, 89.50)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	-0.79 (2.09)
95% CI of LS mean	(-5.07, 3.48)
Week 16 (MMRM)	
n	31
LS mean (SE)	84.23 (2.13)
95% CI of LS mean	(79.88, 88.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	-1.79 (2.13)
95% CI of LS mean	(-6.14, 2.55)
Week 24	
n	31
Mean (SD)	84.23 (18.54)
Absolute Change at Week 24	
n	31
Mean (SD)	-1.79 (19.69)
Week 24 (MMRM)	
n	31
LS mean (SE)	84.23 (3.30)
95% CI of LS mean	(77.45, 91.01)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	-1.79 (3.30)
95% CI of LS mean	(-8.57, 4.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	-1.79 (2.05)
95% CI of LS mean	(-6.01, 2.43)
P-value	0.3903

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	86.38 (13.85)
Week 4 (MMRM)	
n	62
LS mean (SE)	83.33 (1.70)
95% CI of LS mean	(79.93, 86.74)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	-3.05 (1.70)
95% CI of LS mean	(-6.45, 0.36)
Week 8 (MMRM)	
n	62
LS mean (SE)	86.20 (1.50)
95% CI of LS mean	(83.20, 89.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	-0.18 (1.50)
95% CI of LS mean	(-3.18, 2.82)
Week 12 (MMRM)	
n	61
LS mean (SE)	86.72 (1.55)
95% CI of LS mean	(83.61, 89.83)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	0.34 (1.55)
95% CI of LS mean	(-2.77, 3.45)
Week 16 (MMRM)	
n	62
LS mean (SE)	89.07 (1.25)
95% CI of LS mean	(86.56, 91.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	2.69 (1.25)
95% CI of LS mean	(0.18, 5.20)
Week 24	
n	62
Mean (SD)	87.46 (17.01)
Absolute Change at Week 24	
n	62
Mean (SD)	1.08 (17.16)
Week 24 (MMRM)	
n	62
LS mean (SE)	87.46 (2.06)
95% CI of LS mean	(83.33, 91.58)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	1.08 (2.06)
95% CI of LS mean	(-3.05, 5.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	1.88 (1.34)
95% CI of LS mean	(-0.81, 4.57)
P-value	0.1669

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	86.67 (14.63)
Week 4 (MMRM)	
n	10
LS mean (SE)	78.89 (3.67)
95% CI of LS mean	(70.58, 87.20)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	-7.78 (3.67)
95% CI of LS mean	(-16.09, 0.53)
Week 8 (MMRM)	
n	10
LS mean (SE)	86.67 (2.38)
95% CI of LS mean	(81.13, 92.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	0.00 (2.38)
95% CI of LS mean	(-5.54, 5.54)
Week 12 (MMRM)	
n	10
LS mean (SE)	87.78 (4.33)
95% CI of LS mean	(77.60, 97.96)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	1.11 (4.33)
95% CI of LS mean	(-9.07, 11.29)
Week 16 (MMRM)	
n	10
LS mean (SE)	87.78 (3.83)
95% CI of LS mean	(78.63, 96.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	1.11 (3.83)
95% CI of LS mean	(-8.04, 10.26)
Week 24	
n	10
Mean (SD)	87.78 (16.10)
Absolute Change at Week 24	
n	10
Mean (SD)	1.11 (8.20)
Week 24 (MMRM)	
n	10
LS mean (SE)	87.78 (2.95)
95% CI of LS mean	(80.94, 94.61)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	1.11 (2.95)
95% CI of LS mean	(-5.72, 7.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	1.11 (2.35)
95% CI of LS mean	(-5.01, 7.23)
P-value	0.6567

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	92.99 (10.28)
Week 4 (MMRM)	
n	44
LS mean (SE)	91.76 (1.73)
95% CI of LS mean	(88.27, 95.25)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	-1.23 (1.73)
95% CI of LS mean	(-4.72, 2.26)
Week 8 (MMRM)	
n	44
LS mean (SE)	89.20 (1.86)
95% CI of LS mean	(85.45, 92.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	-3.79 (1.86)
95% CI of LS mean	(-7.54, -0.03)
Week 12 (MMRM)	
n	43
LS mean (SE)	93.27 (1.33)
95% CI of LS mean	(90.59, 95.95)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	0.28 (1.33)
95% CI of LS mean	(-2.40, 2.96)
Week 16 (MMRM)	
n	44
LS mean (SE)	93.47 (1.84)
95% CI of LS mean	(89.76, 97.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	0.47 (1.84)
95% CI of LS mean	(-3.24, 4.18)
Week 24	
n	44
Mean (SD)	93.47 (12.43)
Absolute Change at Week 24	
n	44
Mean (SD)	0.47 (8.91)
Week 24 (MMRM)	
n	44
LS mean (SE)	93.47 (1.38)
95% CI of LS mean	(90.68, 96.25)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	0.47 (1.38)
95% CI of LS mean	(-2.31, 3.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	0.47 (1.24)
95% CI of LS mean	(-2.02, 2.97)
P-value	0.7038

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	90.44 (16.56)
Week 4 (MMRM)	
n	34
LS mean (SE)	90.07 (2.16)
95% CI of LS mean	(85.67, 94.48)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	-0.37 (2.16)
95% CI of LS mean	(-4.77, 4.04)
Week 8 (MMRM)	
n	34
LS mean (SE)	91.32 (1.87)
95% CI of LS mean	(87.48, 95.15)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	0.88 (1.87)
95% CI of LS mean	(-2.96, 4.71)
Week 12 (MMRM)	
n	34
LS mean (SE)	95.83 (0.74)
95% CI of LS mean	(94.32, 97.35)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	5.39 (0.74)
95% CI of LS mean	(3.88, 6.91)
Week 16 (MMRM)	
n	34
LS mean (SE)	95.10 (1.45)
95% CI of LS mean	(92.15, 98.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	4.66 (1.45)
95% CI of LS mean	(1.71, 7.61)
Week 24	
n	34
Mean (SD)	90.44 (17.36)
Absolute Change at Week 24	
n	34
Mean (SD)	0.00 (14.29)
Week 24 (MMRM)	
n	34
LS mean (SE)	90.44 (2.52)
95% CI of LS mean	(85.32, 95.57)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	0.00 (2.52)
95% CI of LS mean	(-5.13, 5.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	2.33 (1.59)
95% CI of LS mean	(-0.92, 5.58)
P-value	0.1541

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	92.02 (14.11)
Week 4 (MMRM)	
n	47
LS mean (SE)	91.31 (1.44)
95% CI of LS mean	(88.41, 94.22)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	-0.71 (1.44)
95% CI of LS mean	(-3.61, 2.19)
Week 8 (MMRM)	
n	47
LS mean (SE)	90.26 (1.67)
95% CI of LS mean	(86.88, 93.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	-1.76 (1.67)
95% CI of LS mean	(-5.14, 1.62)
Week 12 (MMRM)	
n	47
LS mean (SE)	94.59 (1.07)
95% CI of LS mean	(92.45, 96.74)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	2.57 (1.07)
95% CI of LS mean	(0.42, 4.72)
Week 16 (MMRM)	
n	47
LS mean (SE)	96.28 (0.86)
95% CI of LS mean	(94.52, 98.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	4.26 (0.86)
95% CI of LS mean	(2.50, 6.01)
Week 24	
n	47
Mean (SD)	93.09 (13.83)
Absolute Change at Week 24	
n	47
Mean (SD)	1.06 (8.58)
Week 24 (MMRM)	
n	47
LS mean (SE)	93.09 (1.31)
95% CI of LS mean	(90.43, 95.74)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	1.06 (1.31)
95% CI of LS mean	(-1.59, 3.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	2.66 (0.83)
95% CI of LS mean	(0.99, 4.33)
P-value	0.0024

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	91.67 (12.31)
Week 4 (MMRM)	
n	31
LS mean (SE)	90.59 (2.37)
95% CI of LS mean	(85.75, 95.43)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	-1.08 (2.37)
95% CI of LS mean	(-5.92, 3.77)
Week 8 (MMRM)	
n	31
LS mean (SE)	89.92 (1.93)
95% CI of LS mean	(85.98, 93.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	-1.75 (1.93)
95% CI of LS mean	(-5.68, 2.19)
Week 12 (MMRM)	
n	30
LS mean (SE)	94.25 (1.38)
95% CI of LS mean	(91.43, 97.07)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	2.58 (1.38)
95% CI of LS mean	(-0.24, 5.40)
Week 16 (MMRM)	
n	31
LS mean (SE)	90.99 (2.74)
95% CI of LS mean	(85.39, 96.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	-0.67 (2.74)
95% CI of LS mean	(-6.27, 4.93)
Week 24	
n	31
Mean (SD)	90.73 (16.20)
Absolute Change at Week 24	
n	31
Mean (SD)	-0.94 (14.93)
Week 24 (MMRM)	
n	31
LS mean (SE)	90.73 (2.64)
95% CI of LS mean	(85.34, 96.12)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	-0.94 (2.64)
95% CI of LS mean	(-6.33, 4.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	-0.81 (2.04)
95% CI of LS mean	(-4.98, 3.36)
P-value	0.6954

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	90.32 (14.49)
Week 4 (MMRM)	
n	62
LS mean (SE)	90.12 (1.46)
95% CI of LS mean	(87.19, 93.05)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	-0.20 (1.46)
95% CI of LS mean	(-3.13, 2.73)
Week 8 (MMRM)	
n	62
LS mean (SE)	88.72 (1.48)
95% CI of LS mean	(85.75, 91.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	-1.60 (1.48)
95% CI of LS mean	(-4.57, 1.37)
Week 12 (MMRM)	
n	61
LS mean (SE)	93.68 (0.98)
95% CI of LS mean	(91.72, 95.65)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	3.36 (0.98)
95% CI of LS mean	(1.39, 5.32)
Week 16 (MMRM)	
n	62
LS mean (SE)	93.68 (1.33)
95% CI of LS mean	(91.02, 96.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	3.36 (1.33)
95% CI of LS mean	(0.70, 6.02)
Week 24	
n	62
Mean (SD)	90.32 (16.05)
Absolute Change at Week 24	
n	62
Mean (SD)	0.00 (12.83)
Week 24 (MMRM)	
n	62
LS mean (SE)	90.32 (1.61)
95% CI of LS mean	(87.09, 93.55)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	0.00 (1.61)
95% CI of LS mean	(-3.23, 3.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	1.68 (1.12)
95% CI of LS mean	(-0.56, 3.92)
P-value	0.1383

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	97.50 (4.03)
Week 4 (MMRM)	
n	10
LS mean (SE)	91.25 (3.12)
95% CI of LS mean	(84.66, 97.84)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	-6.25 (3.12)
95% CI of LS mean	(-12.84, 0.34)
Week 8 (MMRM)	
n	10
LS mean (SE)	95.42 (3.12)
95% CI of LS mean	(88.83, 102.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	-2.08 (3.12)
95% CI of LS mean	(-8.67, 4.50)
Week 12 (MMRM)	
n	10
LS mean (SE)	95.83 (3.12)
95% CI of LS mean	(89.25, 102.42)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	-1.67 (3.12)
95% CI of LS mean	(-8.25, 4.92)
Week 16 (MMRM)	
n	10
LS mean (SE)	93.75 (3.12)
95% CI of LS mean	(87.16, 100.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	-3.75 (3.12)
95% CI of LS mean	(-10.34, 2.84)
Week 24	
n	10
Mean (SD)	98.75 (2.01)
Absolute Change at Week 24	
n	10
Mean (SD)	1.25 (2.81)
Week 24 (MMRM)	
n	10
LS mean (SE)	98.75 (3.12)
95% CI of LS mean	(92.16, 105.34)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	1.25 (3.12)
95% CI of LS mean	(-5.34, 7.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	-1.25 (2.73)
95% CI of LS mean	(-7.28, 4.78)
P-value	0.6558

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	82.77 (17.65)
Week 4 (MMRM)	
n	44
LS mean (SE)	84.09 (2.11)
95% CI of LS mean	(79.83, 88.35)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	1.33 (2.11)
95% CI of LS mean	(-2.93, 5.58)
Week 8 (MMRM)	
n	44
LS mean (SE)	81.82 (2.32)
95% CI of LS mean	(77.14, 86.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	-0.95 (2.32)
95% CI of LS mean	(-5.62, 3.73)
Week 12 (MMRM)	
n	43
LS mean (SE)	84.63 (1.62)
95% CI of LS mean	(81.34, 87.92)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	1.87 (1.62)
95% CI of LS mean	(-1.42, 5.16)
Week 16 (MMRM)	
n	44
LS mean (SE)	84.66 (2.27)
95% CI of LS mean	(80.08, 89.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	1.89 (2.27)
95% CI of LS mean	(-2.69, 6.47)
Week 24	
n	44
Mean (SD)	86.17 (15.56)
Absolute Change at Week 24	
n	44
Mean (SD)	3.41 (14.64)
Week 24 (MMRM)	
n	44
LS mean (SE)	86.17 (1.90)
95% CI of LS mean	(82.33, 90.01)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	3.41 (1.90)
95% CI of LS mean	(-0.43, 7.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	2.65 (1.83)
95% CI of LS mean	(-1.05, 6.35)
P-value	0.1550

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	77.45 (16.86)
Week 4 (MMRM)	
n	34
LS mean (SE)	80.39 (2.50)
95% CI of LS mean	(75.28, 85.50)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	2.94 (2.50)
95% CI of LS mean	(-2.17, 8.05)
Week 8 (MMRM)	
n	34
LS mean (SE)	80.88 (2.65)
95% CI of LS mean	(75.45, 86.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	3.43 (2.65)
95% CI of LS mean	(-2.00, 8.87)
Week 12 (MMRM)	
n	34
LS mean (SE)	83.58 (2.52)
95% CI of LS mean	(78.45, 88.71)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	6.13 (2.52)
95% CI of LS mean	(1.00, 11.26)
Week 16 (MMRM)	
n	34
LS mean (SE)	85.54 (2.23)
95% CI of LS mean	(81.00, 90.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	8.09 (2.23)
95% CI of LS mean	(3.55, 12.63)
Week 24	
n	34
Mean (SD)	78.19 (18.00)
Absolute Change at Week 24	
n	34
Mean (SD)	0.74 (16.46)
Week 24 (MMRM)	
n	34
LS mean (SE)	78.19 (2.60)
95% CI of LS mean	(72.89, 83.48)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	0.74 (2.60)
95% CI of LS mean	(-4.56, 6.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	4.41 (2.04)
95% CI of LS mean	(0.25, 8.58)
P-value	0.0386

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	78.90 (18.78)
Week 4 (MMRM)	
n	47
LS mean (SE)	82.09 (1.80)
95% CI of LS mean	(78.45, 85.73)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	3.19 (1.80)
95% CI of LS mean	(-0.45, 6.83)
Week 8 (MMRM)	
n	47
LS mean (SE)	79.96 (2.39)
95% CI of LS mean	(75.15, 84.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	1.06 (2.39)
95% CI of LS mean	(-3.75, 5.88)
Week 12 (MMRM)	
n	47
LS mean (SE)	83.57 (1.87)
95% CI of LS mean	(79.78, 87.36)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	4.67 (1.87)
95% CI of LS mean	(0.88, 8.46)
Week 16 (MMRM)	
n	47
LS mean (SE)	85.99 (2.08)
95% CI of LS mean	(81.80, 90.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	7.09 (2.08)
95% CI of LS mean	(2.90, 11.29)
Week 24	
n	47
Mean (SD)	82.62 (16.92)
Absolute Change at Week 24	
n	47
Mean (SD)	3.72 (15.43)
Week 24 (MMRM)	
n	47
LS mean (SE)	82.62 (1.93)
95% CI of LS mean	(78.73, 86.52)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	3.72 (1.93)
95% CI of LS mean	(-0.17, 7.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	5.41 (1.85)
95% CI of LS mean	(1.67, 9.14)
P-value	0.0056

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	82.80 (15.05)
Week 4 (MMRM)	
n	31
LS mean (SE)	83.06 (3.04)
95% CI of LS mean	(76.85, 89.28)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	0.27 (3.04)
95% CI of LS mean	(-5.94, 6.48)
Week 8 (MMRM)	
n	31
LS mean (SE)	83.60 (2.36)
95% CI of LS mean	(78.76, 88.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	0.81 (2.36)
95% CI of LS mean	(-4.03, 5.65)
Week 12 (MMRM)	
n	30
LS mean (SE)	85.09 (2.18)
95% CI of LS mean	(80.63, 89.54)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	2.29 (2.18)
95% CI of LS mean	(-2.17, 6.75)
Week 16 (MMRM)	
n	31
LS mean (SE)	83.60 (2.52)
95% CI of LS mean	(78.46, 88.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	0.81 (2.52)
95% CI of LS mean	(-4.34, 5.95)
Week 24	
n	31
Mean (SD)	82.80 (17.47)
Absolute Change at Week 24	
n	31
Mean (SD)	0.00 (15.37)
Week 24 (MMRM)	
n	31
LS mean (SE)	82.80 (2.67)
95% CI of LS mean	(77.34, 88.25)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	0.00 (2.67)
95% CI of LS mean	(-5.46, 5.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	0.40 (1.90)
95% CI of LS mean	(-3.49, 4.30)
P-value	0.8334

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	79.84 (18.02)
Week 4 (MMRM)	
n	62
LS mean (SE)	81.59 (1.92)
95% CI of LS mean	(77.74, 85.43)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	1.75 (1.92)
95% CI of LS mean	(-2.10, 5.60)
Week 8 (MMRM)	
n	62
LS mean (SE)	80.78 (2.04)
95% CI of LS mean	(76.71, 84.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	0.94 (2.04)
95% CI of LS mean	(-3.13, 5.01)
Week 12 (MMRM)	
n	61
LS mean (SE)	83.20 (1.68)
95% CI of LS mean	(79.83, 86.57)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	3.36 (1.68)
95% CI of LS mean	(-0.01, 6.73)
Week 16 (MMRM)	
n	62
LS mean (SE)	84.14 (1.76)
95% CI of LS mean	(80.61, 87.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	4.30 (1.76)
95% CI of LS mean	(0.77, 7.83)
Week 24	
n	62
Mean (SD)	81.32 (17.83)
Absolute Change at Week 24	
n	62
Mean (SD)	1.48 (16.22)
Week 24 (MMRM)	
n	62
LS mean (SE)	81.32 (1.82)
95% CI of LS mean	(77.68, 84.96)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	1.48 (1.82)
95% CI of LS mean	(-2.16, 5.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	2.89 (1.50)
95% CI of LS mean	(-0.12, 5.90)
P-value	0.0592

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	81.67 (18.76)
Week 4 (MMRM)	
n	10
LS mean (SE)	86.67 (3.36)
95% CI of LS mean	(78.62, 94.71)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	5.00 (3.36)
95% CI of LS mean	(-3.04, 13.04)
Week 8 (MMRM)	
n	10
LS mean (SE)	83.33 (3.95)
95% CI of LS mean	(74.38, 92.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	1.67 (3.95)
95% CI of LS mean	(-7.29, 10.62)
Week 12 (MMRM)	
n	10
LS mean (SE)	85.83 (2.36)
95% CI of LS mean	(80.18, 91.49)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	4.17 (2.36)
95% CI of LS mean	(-1.49, 9.82)
Week 16 (MMRM)	
n	10
LS mean (SE)	87.50 (6.25)
95% CI of LS mean	(73.09, 101.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	5.83 (6.25)
95% CI of LS mean	(-8.58, 20.25)
Week 24	
n	10
Mean (SD)	86.67 (15.32)
Absolute Change at Week 24	
n	10
Mean (SD)	5.00 (14.27)
Week 24 (MMRM)	
n	10
LS mean (SE)	86.67 (4.23)
95% CI of LS mean	(76.80, 96.53)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	5.00 (4.23)
95% CI of LS mean	(-4.86, 14.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	5.42 (4.71)
95% CI of LS mean	(-5.63, 16.46)
P-value	0.2862

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	72.73 (23.17)
Week 4 (MMRM)	
n	44
LS mean (SE)	77.53 (1.91)
95% CI of LS mean	(73.67, 81.38)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	4.80 (1.91)
95% CI of LS mean	(0.94, 8.65)
Week 8 (MMRM)	
n	44
LS mean (SE)	80.56 (2.74)
95% CI of LS mean	(75.01, 86.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	7.83 (2.74)
95% CI of LS mean	(2.28, 13.38)
Week 12 (MMRM)	
n	43
LS mean (SE)	78.67 (2.61)
95% CI of LS mean	(73.40, 83.94)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	5.94 (2.61)
95% CI of LS mean	(0.67, 11.22)
Week 16 (MMRM)	
n	44
LS mean (SE)	78.79 (2.08)
95% CI of LS mean	(74.60, 82.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	6.06 (2.08)
95% CI of LS mean	(1.87, 10.25)
Week 24	
n	44
Mean (SD)	80.56 (21.85)
Absolute Change at Week 24	
n	44
Mean (SD)	7.83 (20.97)
Week 24 (MMRM)	
n	44
LS mean (SE)	80.56 (2.64)
95% CI of LS mean	(75.21, 85.90)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	7.83 (2.64)
95% CI of LS mean	(2.49, 13.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	6.94 (1.99)
95% CI of LS mean	(2.91, 10.98)
P-value	0.0012

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	65.03 (17.76)
Week 4 (MMRM)	
n	34
LS mean (SE)	74.51 (2.41)
95% CI of LS mean	(69.60, 79.42)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	9.48 (2.41)
95% CI of LS mean	(4.57, 14.39)
Week 8 (MMRM)	
n	34
LS mean (SE)	74.84 (3.19)
95% CI of LS mean	(68.33, 81.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	9.80 (3.19)
95% CI of LS mean	(3.29, 16.31)
Week 12 (MMRM)	
n	34
LS mean (SE)	71.90 (3.26)
95% CI of LS mean	(65.27, 78.52)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	6.86 (3.26)
95% CI of LS mean	(0.23, 13.49)
Week 16 (MMRM)	
n	34
LS mean (SE)	74.84 (2.51)
95% CI of LS mean	(69.71, 79.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	9.80 (2.51)
95% CI of LS mean	(4.68, 14.93)
Week 24	
n	34
Mean (SD)	75.16 (19.92)
Absolute Change at Week 24	
n	34
Mean (SD)	10.13 (16.50)
Week 24 (MMRM)	
n	34
LS mean (SE)	75.16 (2.63)
95% CI of LS mean	(69.81, 80.52)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	10.13 (2.63)
95% CI of LS mean	(4.78, 15.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	9.97 (2.35)
95% CI of LS mean	(5.17, 14.76)
P-value	0.0002

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	70.21 (21.12)
Week 4 (MMRM)	
n	47
LS mean (SE)	77.07 (2.00)
95% CI of LS mean	(73.04, 81.10)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	6.86 (2.00)
95% CI of LS mean	(2.83, 10.88)
Week 8 (MMRM)	
n	47
LS mean (SE)	78.01 (2.69)
95% CI of LS mean	(72.60, 83.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	7.80 (2.69)
95% CI of LS mean	(2.39, 13.21)
Week 12 (MMRM)	
n	47
LS mean (SE)	74.47 (2.73)
95% CI of LS mean	(68.97, 79.97)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	4.26 (2.73)
95% CI of LS mean	(-1.25, 9.76)
Week 16 (MMRM)	
n	47
LS mean (SE)	80.14 (2.23)
95% CI of LS mean	(75.66, 84.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	9.93 (2.23)
95% CI of LS mean	(5.44, 14.41)
Week 24	
n	47
Mean (SD)	79.20 (19.33)
Absolute Change at Week 24	
n	47
Mean (SD)	8.98 (20.15)
Week 24 (MMRM)	
n	47
LS mean (SE)	79.20 (2.50)
95% CI of LS mean	(74.16, 84.23)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	8.98 (2.50)
95% CI of LS mean	(3.95, 14.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	9.46 (2.12)
95% CI of LS mean	(5.17, 13.74)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	68.10 (21.61)
Week 4 (MMRM)	
n	31
LS mean (SE)	74.91 (2.30)
95% CI of LS mean	(70.18, 79.64)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	6.81 (2.30)
95% CI of LS mean	(2.08, 11.54)
Week 8 (MMRM)	
n	31
LS mean (SE)	78.14 (3.81)
95% CI of LS mean	(70.31, 85.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	10.04 (3.81)
95% CI of LS mean	(2.21, 17.87)
Week 12 (MMRM)	
n	30
LS mean (SE)	77.68 (3.17)
95% CI of LS mean	(71.20, 84.16)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	9.58 (3.17)
95% CI of LS mean	(3.10, 16.06)
Week 16 (MMRM)	
n	31
LS mean (SE)	72.40 (1.99)
95% CI of LS mean	(68.31, 76.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	4.30 (1.99)
95% CI of LS mean	(0.21, 8.40)
Week 24	
n	31
Mean (SD)	76.70 (23.72)
Absolute Change at Week 24	
n	31
Mean (SD)	8.60 (17.62)
Week 24 (MMRM)	
n	31
LS mean (SE)	76.70 (3.11)
95% CI of LS mean	(70.34, 83.07)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	8.60 (3.11)
95% CI of LS mean	(2.24, 14.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	6.45 (2.19)
95% CI of LS mean	(1.97, 10.93)
P-value	0.0064

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	67.20 (21.05)
Week 4 (MMRM)	
n	62
LS mean (SE)	75.45 (1.71)
95% CI of LS mean	(72.02, 78.87)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	8.24 (1.71)
95% CI of LS mean	(4.82, 11.67)
Week 8 (MMRM)	
n	62
LS mean (SE)	77.96 (2.48)
95% CI of LS mean	(72.98, 82.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	10.75 (2.48)
95% CI of LS mean	(5.78, 15.73)
Week 12 (MMRM)	
n	61
LS mean (SE)	74.78 (2.33)
95% CI of LS mean	(70.13, 79.43)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	7.58 (2.33)
95% CI of LS mean	(2.93, 12.23)
Week 16 (MMRM)	
n	62
LS mean (SE)	76.70 (1.90)
95% CI of LS mean	(72.89, 80.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	9.50 (1.90)
95% CI of LS mean	(5.69, 13.31)
Week 24	
n	62
Mean (SD)	77.42 (21.57)
Absolute Change at Week 24	
n	62
Mean (SD)	10.22 (18.14)
Week 24 (MMRM)	
n	62
LS mean (SE)	77.42 (2.13)
95% CI of LS mean	(73.16, 81.68)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	10.22 (2.13)
95% CI of LS mean	(5.96, 14.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	9.86 (1.81)
95% CI of LS mean	(6.24, 13.47)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	77.78 (20.95)
Week 4 (MMRM)	
n	10
LS mean (SE)	75.56 (4.33)
95% CI of LS mean	(65.42, 85.69)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	-2.22 (4.33)
95% CI of LS mean	(-12.35, 7.91)
Week 8 (MMRM)	
n	10
LS mean (SE)	73.33 (5.26)
95% CI of LS mean	(61.30, 85.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	-4.44 (5.26)
95% CI of LS mean	(-16.47, 7.58)
Week 12 (MMRM)	
n	10
LS mean (SE)	74.44 (6.30)
95% CI of LS mean	(59.99, 88.90)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	-3.33 (6.30)
95% CI of LS mean	(-17.79, 11.12)
Week 16 (MMRM)	
n	10
LS mean (SE)	73.33 (3.09)
95% CI of LS mean	(66.26, 80.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	-4.44 (3.09)
95% CI of LS mean	(-11.52, 2.63)
Week 24	
n	10
Mean (SD)	76.67 (22.50)
Absolute Change at Week 24	
n	10
Mean (SD)	-1.11 (21.24)
Week 24 (MMRM)	
n	10
LS mean (SE)	76.67 (7.11)
95% CI of LS mean	(60.22, 93.11)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	-1.11 (7.11)
95% CI of LS mean	(-17.56, 15.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	-2.78 (4.45)
95% CI of LS mean	(-13.23, 7.67)
P-value	0.5513

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	78.18 (12.15)
Week 4 (MMRM)	
n	44
LS mean (SE)	76.82 (1.79)
95% CI of LS mean	(73.21, 80.43)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	-1.36 (1.79)
95% CI of LS mean	(-4.97, 2.25)
Week 8 (MMRM)	
n	44
LS mean (SE)	76.82 (1.71)
95% CI of LS mean	(73.37, 80.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	-1.36 (1.71)
95% CI of LS mean	(-4.81, 2.09)
Week 12 (MMRM)	
n	43
LS mean (SE)	78.85 (1.46)
95% CI of LS mean	(75.89, 81.80)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	0.66 (1.46)
95% CI of LS mean	(-2.29, 3.62)
Week 16 (MMRM)	
n	44
LS mean (SE)	80.15 (1.79)
95% CI of LS mean	(76.53, 83.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	1.97 (1.79)
95% CI of LS mean	(-1.65, 5.59)
Week 24	
n	44
Mean (SD)	78.79 (12.88)
Absolute Change at Week 24	
n	44
Mean (SD)	0.61 (12.76)
Week 24 (MMRM)	
n	44
LS mean (SE)	78.79 (1.74)
95% CI of LS mean	(75.27, 82.30)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	0.61 (1.74)
95% CI of LS mean	(-2.91, 4.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	1.29 (1.42)
95% CI of LS mean	(-1.58, 4.15)
P-value	0.3694

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	74.71 (12.80)
Week 4 (MMRM)	
n	34
LS mean (SE)	73.14 (2.27)
95% CI of LS mean	(68.52, 77.75)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	-1.57 (2.27)
95% CI of LS mean	(-6.18, 3.04)
Week 8 (MMRM)	
n	34
LS mean (SE)	73.33 (1.32)
95% CI of LS mean	(70.65, 76.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	-1.37 (1.32)
95% CI of LS mean	(-4.05, 1.31)
Week 12 (MMRM)	
n	34
LS mean (SE)	75.88 (2.08)
95% CI of LS mean	(71.65, 80.12)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	1.18 (2.08)
95% CI of LS mean	(-3.06, 5.41)
Week 16 (MMRM)	
n	34
LS mean (SE)	76.67 (1.73)
95% CI of LS mean	(73.14, 80.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	1.96 (1.73)
95% CI of LS mean	(-1.57, 5.49)
Week 24	
n	34
Mean (SD)	71.96 (14.93)
Absolute Change at Week 24	
n	34
Mean (SD)	-2.75 (15.32)
Week 24 (MMRM)	
n	34
LS mean (SE)	71.96 (2.38)
95% CI of LS mean	(67.12, 76.80)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	-2.75 (2.38)
95% CI of LS mean	(-7.59, 2.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	-0.39 (1.76)
95% CI of LS mean	(-3.97, 3.19)
P-value	0.8250

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	75.60 (12.91)
Week 4 (MMRM)	
n	47
LS mean (SE)	75.18 (1.80)
95% CI of LS mean	(71.56, 78.80)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	-0.43 (1.80)
95% CI of LS mean	(-4.05, 3.19)
Week 8 (MMRM)	
n	47
LS mean (SE)	74.33 (1.39)
95% CI of LS mean	(71.53, 77.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	-1.28 (1.39)
95% CI of LS mean	(-4.07, 1.52)
Week 12 (MMRM)	
n	47
LS mean (SE)	76.03 (1.54)
95% CI of LS mean	(72.92, 79.14)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	0.43 (1.54)
95% CI of LS mean	(-2.68, 3.53)
Week 16 (MMRM)	
n	47
LS mean (SE)	79.15 (1.38)
95% CI of LS mean	(76.38, 81.92)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	3.55 (1.38)
95% CI of LS mean	(0.78, 6.32)
Week 24	
n	47
Mean (SD)	75.60 (12.99)
Absolute Change at Week 24	
n	47
Mean (SD)	0.00 (12.20)
Week 24 (MMRM)	
n	47
LS mean (SE)	75.60 (1.59)
95% CI of LS mean	(72.40, 78.81)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	0.00 (1.59)
95% CI of LS mean	(-3.21, 3.21)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	1.77 (1.18)
95% CI of LS mean	(-0.60, 4.15)
P-value	0.1401

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	78.28 (11.80)
Week 4 (MMRM)	
n	31
LS mean (SE)	75.27 (2.24)
95% CI of LS mean	(70.68, 79.86)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	-3.01 (2.24)
95% CI of LS mean	(-7.60, 1.58)
Week 8 (MMRM)	
n	31
LS mean (SE)	76.77 (1.88)
95% CI of LS mean	(72.92, 80.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	-1.51 (1.88)
95% CI of LS mean	(-5.36, 2.35)
Week 12 (MMRM)	
n	30
LS mean (SE)	79.91 (2.04)
95% CI of LS mean	(75.74, 84.09)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	1.63 (2.04)
95% CI of LS mean	(-2.54, 5.81)
Week 16 (MMRM)	
n	31
LS mean (SE)	77.85 (2.36)
95% CI of LS mean	(73.02, 82.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	-0.43 (2.36)
95% CI of LS mean	(-5.26, 4.40)
Week 24	
n	31
Mean (SD)	76.13 (15.94)
Absolute Change at Week 24	
n	31
Mean (SD)	-2.15 (16.37)
Week 24 (MMRM)	
n	31
LS mean (SE)	76.13 (2.75)
95% CI of LS mean	(70.51, 81.74)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	-2.15 (2.75)
95% CI of LS mean	(-7.77, 3.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	-1.29 (2.16)
95% CI of LS mean	(-5.71, 3.13)
P-value	0.5549

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	75.59 (12.07)
Week 4 (MMRM)	
n	62
LS mean (SE)	73.87 (1.41)
95% CI of LS mean	(71.04, 76.70)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	-1.72 (1.41)
95% CI of LS mean	(-4.55, 1.11)
Week 8 (MMRM)	
n	62
LS mean (SE)	74.41 (1.22)
95% CI of LS mean	(71.98, 76.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	-1.18 (1.22)
95% CI of LS mean	(-3.62, 1.25)
Week 12 (MMRM)	
n	61
LS mean (SE)	76.19 (1.32)
95% CI of LS mean	(73.55, 78.83)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	0.60 (1.32)
95% CI of LS mean	(-2.04, 3.24)
Week 16 (MMRM)	
n	62
LS mean (SE)	76.34 (1.30)
95% CI of LS mean	(73.74, 78.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	0.75 (1.30)
95% CI of LS mean	(-1.85, 3.36)
Week 24	
n	62
Mean (SD)	73.98 (13.43)
Absolute Change at Week 24	
n	62
Mean (SD)	-1.61 (14.32)
Week 24 (MMRM)	
n	62
LS mean (SE)	73.98 (1.59)
95% CI of LS mean	(70.79, 77.17)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	-1.61 (1.59)
95% CI of LS mean	(-4.80, 1.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	-0.43 (1.21)
95% CI of LS mean	(-2.86, 2.00)
P-value	0.7240

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	79.33 (12.75)
Week 4 (MMRM)	
n	10
LS mean (SE)	77.33 (5.81)
95% CI of LS mean	(64.15, 90.52)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	-2.00 (5.81)
95% CI of LS mean	(-15.19, 11.19)
Week 8 (MMRM)	
n	10
LS mean (SE)	79.33 (3.13)
95% CI of LS mean	(71.70, 86.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	0.00 (3.13)
95% CI of LS mean	(-7.63, 7.63)
Week 12 (MMRM)	
n	10
LS mean (SE)	82.00 (4.91)
95% CI of LS mean	(70.16, 93.84)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	2.67 (4.91)
95% CI of LS mean	(-9.17, 14.50)
Week 16 (MMRM)	
n	10
LS mean (SE)	87.33 (3.33)
95% CI of LS mean	(79.76, 94.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	8.00 (3.33)
95% CI of LS mean	(0.42, 15.58)
Week 24	
n	10
Mean (SD)	81.33 (16.87)
Absolute Change at Week 24	
n	10
Mean (SD)	2.00 (13.35)
Week 24 (MMRM)	
n	10
LS mean (SE)	81.33 (4.46)
95% CI of LS mean	(71.05, 91.61)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	2.00 (4.46)
95% CI of LS mean	(-8.28, 12.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	5.00 (2.12)
95% CI of LS mean	(-0.19, 10.19)
P-value	0.0563

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	70.45 (35.38)
Week 4 (MMRM)	
n	44
LS mean (SE)	70.45 (3.70)
95% CI of LS mean	(62.99, 77.92)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	0.00 (3.70)
95% CI of LS mean	(-7.46, 7.46)
Week 8 (MMRM)	
n	44
LS mean (SE)	78.03 (3.54)
95% CI of LS mean	(70.88, 85.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	7.58 (3.54)
95% CI of LS mean	(0.43, 14.72)
Week 12 (MMRM)	
n	43
LS mean (SE)	75.82 (3.42)
95% CI of LS mean	(68.91, 82.74)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	5.37 (3.42)
95% CI of LS mean	(-1.54, 12.28)
Week 16 (MMRM)	
n	44
LS mean (SE)	75.00 (3.64)
95% CI of LS mean	(67.65, 82.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	4.55 (3.64)
95% CI of LS mean	(-2.81, 11.90)
Week 24	
n	44
Mean (SD)	71.21 (35.65)
Absolute Change at Week 24	
n	44
Mean (SD)	0.76 (22.14)
Week 24 (MMRM)	
n	44
LS mean (SE)	71.21 (3.27)
95% CI of LS mean	(64.61, 77.82)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	0.76 (3.27)
95% CI of LS mean	(-5.85, 7.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	2.65 (2.79)
95% CI of LS mean	(-2.99, 8.29)
P-value	0.3478

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	67.65 (36.22)
Week 4 (MMRM)	
n	34
LS mean (SE)	70.59 (4.61)
95% CI of LS mean	(61.18, 80.00)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	2.94 (4.61)
95% CI of LS mean	(-6.47, 12.35)
Week 8 (MMRM)	
n	34
LS mean (SE)	71.57 (4.03)
95% CI of LS mean	(63.36, 79.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	3.92 (4.03)
95% CI of LS mean	(-4.29, 12.13)
Week 12 (MMRM)	
n	34
LS mean (SE)	70.59 (4.16)
95% CI of LS mean	(62.10, 79.07)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	2.94 (4.16)
95% CI of LS mean	(-5.54, 11.42)
Week 16 (MMRM)	
n	34
LS mean (SE)	73.53 (4.00)
95% CI of LS mean	(65.38, 81.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	5.88 (4.00)
95% CI of LS mean	(-2.26, 14.03)
Week 24	
n	34
Mean (SD)	78.43 (31.66)
Absolute Change at Week 24	
n	34
Mean (SD)	10.78 (33.56)
Week 24 (MMRM)	
n	34
LS mean (SE)	78.43 (4.75)
95% CI of LS mean	(68.75, 88.11)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	10.78 (4.75)
95% CI of LS mean	(1.10, 20.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	8.33 (4.03)
95% CI of LS mean	(0.13, 16.54)
P-value	0.0468

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	71.63 (35.43)
Week 4 (MMRM)	
n	47
LS mean (SE)	72.34 (4.10)
95% CI of LS mean	(64.09, 80.59)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	0.71 (4.10)
95% CI of LS mean	(-7.54, 8.96)
Week 8 (MMRM)	
n	47
LS mean (SE)	79.43 (3.40)
95% CI of LS mean	(72.57, 86.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	7.80 (3.40)
95% CI of LS mean	(0.94, 14.66)
Week 12 (MMRM)	
n	47
LS mean (SE)	76.60 (3.55)
95% CI of LS mean	(69.44, 83.75)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	4.96 (3.55)
95% CI of LS mean	(-2.19, 12.12)
Week 16 (MMRM)	
n	47
LS mean (SE)	80.14 (3.41)
95% CI of LS mean	(73.26, 87.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	8.51 (3.41)
95% CI of LS mean	(1.63, 15.39)
Week 24	
n	47
Mean (SD)	80.14 (29.21)
Absolute Change at Week 24	
n	47
Mean (SD)	8.51 (29.87)
Week 24 (MMRM)	
n	47
LS mean (SE)	80.14 (3.50)
95% CI of LS mean	(73.10, 87.18)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	8.51 (3.50)
95% CI of LS mean	(1.47, 15.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	8.51 (2.98)
95% CI of LS mean	(2.51, 14.51)
P-value	0.0064

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	65.59 (35.99)
Week 4 (MMRM)	
n	31
LS mean (SE)	67.74 (3.35)
95% CI of LS mean	(60.89, 74.60)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	2.15 (3.35)
95% CI of LS mean	(-4.70, 9.01)
Week 8 (MMRM)	
n	31
LS mean (SE)	68.82 (3.99)
95% CI of LS mean	(60.64, 76.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	3.23 (3.99)
95% CI of LS mean	(-4.95, 11.40)
Week 12 (MMRM)	
n	30
LS mean (SE)	68.88 (4.33)
95% CI of LS mean	(60.02, 77.73)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	3.28 (4.33)
95% CI of LS mean	(-5.57, 12.14)
Week 16 (MMRM)	
n	31
LS mean (SE)	65.59 (4.30)
95% CI of LS mean	(56.76, 74.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	0.00 (4.30)
95% CI of LS mean	(-8.83, 8.83)
Week 24	
n	31
Mean (SD)	65.59 (38.95)
Absolute Change at Week 24	
n	31
Mean (SD)	0.00 (24.34)
Week 24 (MMRM)	
n	31
LS mean (SE)	65.59 (4.31)
95% CI of LS mean	(56.78, 74.40)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	0.00 (4.31)
95% CI of LS mean	(-8.81, 8.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	0.00 (3.63)
95% CI of LS mean	(-7.43, 7.43)
P-value	>0.9999

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	65.05 (37.90)
Week 4 (MMRM)	
n	62
LS mean (SE)	68.28 (3.16)
95% CI of LS mean	(61.96, 74.60)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	3.23 (3.16)
95% CI of LS mean	(-3.10, 9.55)
Week 8 (MMRM)	
n	62
LS mean (SE)	72.58 (3.13)
95% CI of LS mean	(66.31, 78.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	7.53 (3.13)
95% CI of LS mean	(1.25, 13.80)
Week 12 (MMRM)	
n	61
LS mean (SE)	71.50 (3.07)
95% CI of LS mean	(65.36, 77.64)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	6.44 (3.07)
95% CI of LS mean	(0.30, 12.59)
Week 16 (MMRM)	
n	62
LS mean (SE)	70.97 (3.24)
95% CI of LS mean	(64.49, 77.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	5.91 (3.24)
95% CI of LS mean	(-0.57, 12.39)
Week 24	
n	62
Mean (SD)	70.43 (36.27)
Absolute Change at Week 24	
n	62
Mean (SD)	5.38 (29.69)
Week 24 (MMRM)	
n	62
LS mean (SE)	70.43 (3.38)
95% CI of LS mean	(63.67, 77.19)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	5.38 (3.38)
95% CI of LS mean	(-1.39, 12.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	5.65 (2.87)
95% CI of LS mean	(-0.10, 11.39)
P-value	0.0540

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	80.00 (17.21)
Week 4 (MMRM)	
n	10
LS mean (SE)	80.00 (9.31)
95% CI of LS mean	(58.85, 101.15)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	0.00 (9.31)
95% CI of LS mean	(-21.15, 21.15)
Week 8 (MMRM)	
n	10
LS mean (SE)	86.67 (5.39)
95% CI of LS mean	(74.43, 98.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	6.67 (5.39)
95% CI of LS mean	(-5.57, 18.90)
Week 12 (MMRM)	
n	10
LS mean (SE)	76.67 (8.84)
95% CI of LS mean	(56.59, 96.74)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	-3.33 (8.84)
95% CI of LS mean	(-23.41, 16.74)
Week 16 (MMRM)	
n	10
LS mean (SE)	86.67 (4.78)
95% CI of LS mean	(75.43, 97.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	6.67 (4.78)
95% CI of LS mean	(-4.57, 17.90)
Week 24	
n	10
Mean (SD)	90.00 (16.10)
Absolute Change at Week 24	
n	10
Mean (SD)	10.00 (16.10)
Week 24 (MMRM)	
n	10
LS mean (SE)	90.00 (4.26)
95% CI of LS mean	(80.32, 99.68)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	10.00 (4.26)
95% CI of LS mean	(0.32, 19.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	8.33 (3.39)
95% CI of LS mean	(0.28, 16.39)
P-value	0.0444

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Any Pulmonary Exacerbation	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 3.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Pulmonary Exacerbation Requiring Hospitalization	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 3.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Pulmonary Exacerbation Requiring IV Antibiotic Therapy	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 3.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Pulmonary Exacerbation Requiring Hospitalization or IV Antibiotic Therapy	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 3.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 3.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 3.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 3.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 31

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 3.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 3.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA
	N = 10

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 3.2.2.14.1
Study VX21-121-105: Subgroup Factor Test for
Time-to-First Pulmonary Exacerbation during the PEx Analysis Period
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Log-rank test.

Table 3.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.15.1
Study VX21-121-105: Subgroup Factor Test for
Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Log-rank test.

Table 3.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 3.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 3.2.2.16.1
Study VX21-121-105: Subgroup Factor Test for
Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Log-rank test.

Table 3.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 3.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

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Table 3.3.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 78 n (%)
Subjects with any TEAEs	72 (92.31)
Respiratory, thoracic and mediastinal disorders	51 (65.38)
Cough	36 (46.15)
Oropharyngeal pain	13 (16.67)
Nasal congestion	9 (11.54)
Rhinorrhoea	9 (11.54)
Infections and infestations	35 (44.87)
Gastrointestinal disorders	25 (32.05)
Abdominal pain	9 (11.54)
Vomiting	8 (10.26)
General disorders and administration site conditions	22 (28.21)
Pyrexia	16 (20.51)
Investigations	22 (28.21)
Nervous system disorders	17 (21.79)
Headache	14 (17.95)
Injury, poisoning and procedural complications	11 (14.10)
Skin and subcutaneous tissue disorders	9 (11.54)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 78 n (%)
Subjects with any TEAEs	72 (92.31)
Grade 1/Mild	39 (50.00)
Grade 2/Moderate	33 (42.31)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Respiratory, thoracic and mediastinal disorders	51 (65.38)
Grade 1/Mild	35 (44.87)
Grade 2/Moderate	16 (20.51)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Cough	36 (46.15)
Grade 1/Mild	24 (30.77)
Grade 2/Moderate	12 (15.38)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Oropharyngeal pain	13 (16.67)
Grade 1/Mild	13 (16.67)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 78 n (%)
Nasal congestion	9 (11.54)
Grade 1/Mild	9 (11.54)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0
Rhinorrhoea	9 (11.54)
Grade 1/Mild	9 (11.54)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0
Infections and infestations	35 (44.87)
Grade 1/Mild	22 (28.21)
Grade 2/Moderate	13 (16.67)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Gastrointestinal disorders	25 (32.05)
Grade 1/Mild	21 (26.92)
Grade 2/Moderate	4 (5.13)
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 78 n (%)
Abdominal pain	9 (11.54)
Grade 1/Mild	8 (10.26)
Grade 2/Moderate	1 (1.28)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Vomiting	8 (10.26)
Grade 1/Mild	6 (7.69)
Grade 2/Moderate	2 (2.56)
Grade 3/Severe	0
Grade 4/Life Threatening	0
General disorders and administration site conditions	22 (28.21)
Grade 1/Mild	19 (24.36)
Grade 2/Moderate	3 (3.85)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Pyrexia	16 (20.51)
Grade 1/Mild	14 (17.95)
Grade 2/Moderate	2 (2.56)
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 78 n (%)
Investigations	22 (28.21)
Grade 1/Mild	17 (21.79)
Grade 2/Moderate	5 (6.41)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Nervous system disorders	17 (21.79)
Grade 1/Mild	13 (16.67)
Grade 2/Moderate	4 (5.13)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Headache	14 (17.95)
Grade 1/Mild	12 (15.38)
Grade 2/Moderate	2 (2.56)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Injury, poisoning and procedural complications	11 (14.10)
Grade 1/Mild	10 (12.82)
Grade 2/Moderate	1 (1.28)
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 78 n (%)
Skin and subcutaneous tissue disorders	9 (11.54)
Grade 1/Mild	9 (11.54)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.1.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 78 n (%)

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 5% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

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Table 3.3.1.3
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 78 n (%)
Subjects with any Serious TEAEs	5 (6.41)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 5% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.1.4
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 78 n (%)
Subjects with any TEAEs leading to treatment discontinuation	1 (1.28)
General disorders and administration site conditions	1 (1.28)
Fatigue	1 (1.28)
Respiratory, thoracic and mediastinal disorders	1 (1.28)
Cough	1 (1.28)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.1.5
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events - Total and by Severity
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Subjects with any Treatment-emergent Elevated Transaminase Events	4 (5.13)
Subjects with non-severe events (Maximum Grade 1/2)	4 (5.13)
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 3.3.1.6
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events - Total and by Severity
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Subjects with any Treatment-emergent Creatine Kinase Elevation Events	2 (2.56)
Subjects with non-severe events (Maximum Grade 1/2)	2 (2.56)
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 3.3.1.7
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events - Total and by Severity
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Subjects with any Treatment-emergent Rash Events	4 (5.13)
Subjects with non-severe events (Maximum Grade 1/2)	4 (5.13)
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 3.3.1.8
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events - Total and by Severity
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Subjects with any Treatment-emergent Cataract Events	1 (1.28)
Subjects with non-severe events (Maximum Grade 1/2)	1 (1.28)
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 3.3.1.9
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events - Total and by Severity
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Subjects with any Treatment-emergent Hypoglycemia Events	0
Subjects with non-severe events (Maximum Grade 1/2)	0
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 3.3.1.10
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events - Total and by Severity
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Subjects with any Treatment-emergent Neuropsychiatric Events	4 (5.13)
Subjects with non-severe events (Maximum Grade 1/2)	4 (5.13)
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 3.3.1.11
Study VX21-121-105: Summary of Death
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)

No data met the criteria for this table.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.

Table 3.3.1.12
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	13 (16.67)
Subjects with non-severe events (Maximum Grade 1/2)	13 (16.67)
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	2 (2.56)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 3.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
Subjects with any TEAEs	
Sex (Male vs. Female)	0.7417
Region (North America vs. Rest of the World)	0.0384
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.3519
Respiratory, thoracic and mediastinal disorders	
Sex (Male vs. Female)	0.5547
Region (North America vs. Rest of the World)	0.3999
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.3351

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
Cough	
Sex (Male vs. Female)	0.5492
Region (North America vs. Rest of the World)	0.5439
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.4374
Oropharyngeal pain	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.4754

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
Infections and infestations	
Sex (Male vs. Female)	0.1349
Region (North America vs. Rest of the World)	0.1506
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.2436
Gastrointestinal disorders	
Sex (Male vs. Female)	0.9600
Region (North America vs. Rest of the World)	0.5978
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.5560

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
General disorders and administration site conditions	
Sex (Male vs. Female)	0.4742
Region (North America vs. Rest of the World)	0.1583
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.9502
Pyrexia	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.4362
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.9443

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
Investigations	
Sex (Male vs. Female)	0.7647
Region (North America vs. Rest of the World)	0.5183
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.0208
Nervous system disorders	
Sex (Male vs. Female)	0.0111
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.1451

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
Headache	
Sex (Male vs. Female)	0.0204
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.2900
Injury, poisoning and procedural complications	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.6171

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 44 n (%)
Subjects with any TEAEs	41 (93.18)
Respiratory, thoracic and mediastinal disorders	30 (68.18)
Cough	19 (43.18)
Infections and infestations	23 (52.27)
Gastrointestinal disorders	14 (31.82)
Investigations	13 (29.55)
General disorders and administration site conditions	11 (25.00)
Nervous system disorders	5 (11.36)
Headache	4 (9.09)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 34 n (%)
Subjects with any TEAEs	31 (91.18)
Respiratory, thoracic and mediastinal disorders	21 (61.76)
Cough	17 (50.00)
Infections and infestations	12 (35.29)
Nervous system disorders	12 (35.29)
Headache	10 (29.41)
Gastrointestinal disorders	11 (32.35)
General disorders and administration site conditions	11 (32.35)
Investigations	9 (26.47)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 47 n (%)
Subjects with any TEAEs	41 (87.23)
Respiratory, thoracic and mediastinal disorders	29 (61.70)
Cough	23 (48.94)
Infections and infestations	18 (38.30)
General disorders and administration site conditions	16 (34.04)
Pyrexia	11 (23.40)
Gastrointestinal disorders	14 (29.79)
Investigations	12 (25.53)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 31 n (%)
Subjects with any TEAEs	31 (100.00)
Respiratory, thoracic and mediastinal disorders	22 (70.97)
Cough	13 (41.94)
Infections and infestations	17 (54.84)
Gastrointestinal disorders	11 (35.48)
Investigations	10 (32.26)
General disorders and administration site conditions	6 (19.35)
Pyrexia	5 (16.13)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 62 n (%)
Subjects with any TEAEs	57 (91.94)
Respiratory, thoracic and mediastinal disorders	40 (64.52)
Cough	29 (46.77)
Oropharyngeal pain	12 (19.35)
Infections and infestations	25 (40.32)
Gastrointestinal disorders	19 (30.65)
General disorders and administration site conditions	18 (29.03)
Pyrexia	13 (20.97)
Investigations	15 (24.19)
Nervous system disorders	12 (19.35)
Headache	10 (16.13)
Injury, poisoning and procedural complications	10 (16.13)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 10 n (%)
Subjects with any TEAEs	10 (100.00)
Respiratory, thoracic and mediastinal disorders	8 (80.00)
Cough	6 (60.00)
Oropharyngeal pain	1 (10.00)
Infections and infestations	6 (60.00)
Investigations	6 (60.00)
Gastrointestinal disorders	4 (40.00)
Nervous system disorders	4 (40.00)
Headache	3 (30.00)
General disorders and administration site conditions	3 (30.00)
Pyrexia	2 (20.00)
Injury, poisoning and procedural complications	1 (10.00)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.2.1
Study VX21-121-105: Subgroup Factor Test for Grade 3/4/5 TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 44 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 34 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 62 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 10 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.3.1
Study VX21-121-105: Subgroup Factor Test for Serious TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 44 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 34 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 62 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 10 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.4.1
Study VX21-121-105: Subgroup Factor Test for TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 44 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 34 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

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Table 3.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 62 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 10 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

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Table 3.3.2.5.1
Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Elevated Transaminase Events
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.5.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.5.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.5.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 47 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.5.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.5.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.5.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Elevated Transaminase Events by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.6.1
Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Creatine Kinase Events
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.6.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.6.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.6.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.6.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.6.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.6.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Creatine Kinase Elevation Events by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 3.3.2.7.1
Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Rash Events
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.7.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 3.3.2.7.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 3.3.2.7.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.7.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.7.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.7.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Rash Events by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.8.1
Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Cataract Events
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.8.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.8.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.8.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.8.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 3.3.2.8.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.8.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Cataract Events by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.9.1
Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Hypoglycemia Events
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.9.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.9.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.9.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.9.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 31 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.9.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.9.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Hypoglycemia Events by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.10.1
Study VX21-121-105: Subgroup Factor Test for AESI of Treatment-emergent Neuropsychiatric Events
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.10.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.10.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.10.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.10.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 31 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.10.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 3.3.2.10.2
Study VX21-121-105: Summary of AESI: Treatment-emergent Neuropsychiatric Events by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.11.1
Study VX21-121-105: Subgroup Factor Test for Death
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

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Table 3.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.12.1
Study VX21-121-105: Subgroup Factor Test for Treatment-emergent Infective Pulmonary Exacerbation Events
Safety Set

Subgroup	P-value[1]
Subjects with non-severe events (Maximum Grade 1/2)	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.7605
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.7605

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	10 (16.13)
Subjects with non-severe events (Maximum Grade 1/2)	10 (16.13)
Subjects with severe events (Maximum Grade 3/4/5)	-
Subjects with serious events	-

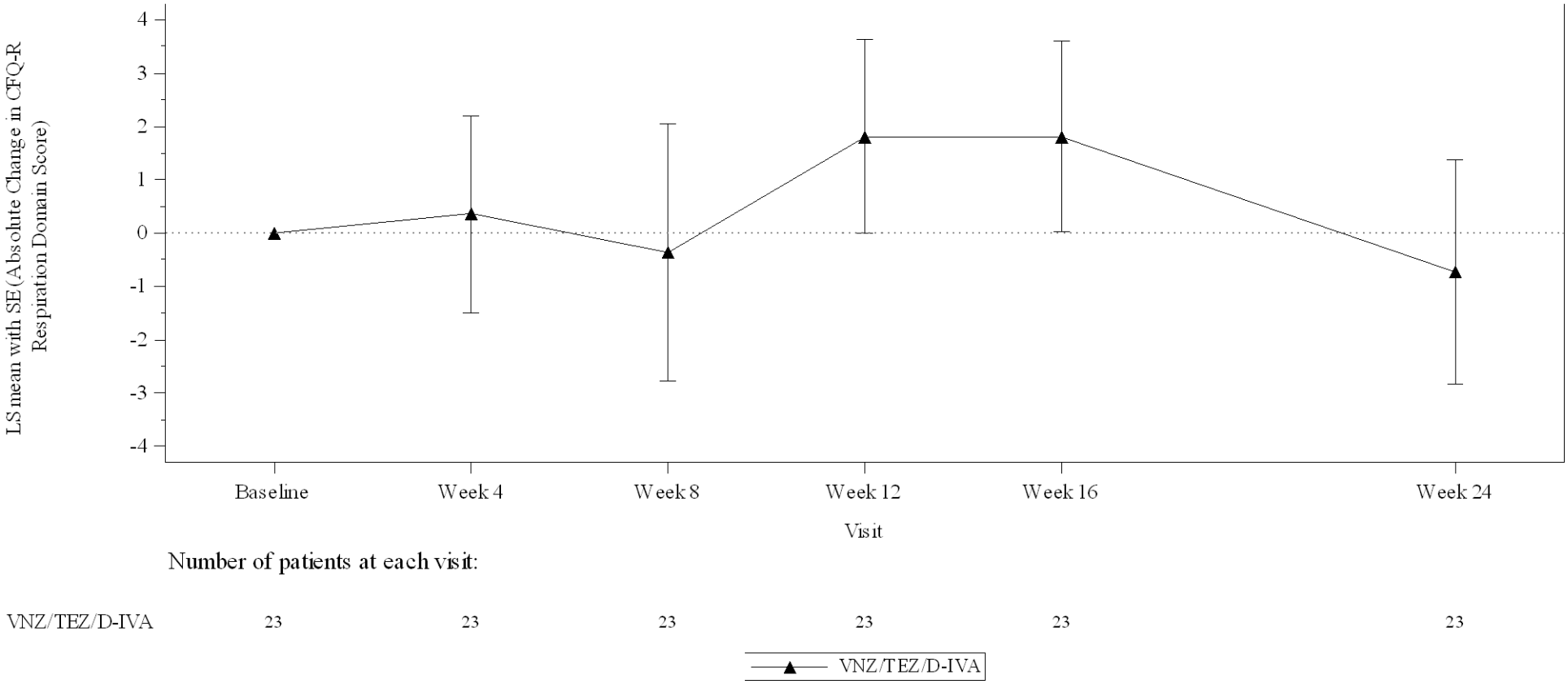
- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	2 (20.00)
Subjects with non-severe events (Maximum Grade 1/2)	2 (20.00)
Subjects with severe events (Maximum Grade 3/4/5)	-
Subjects with serious events	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

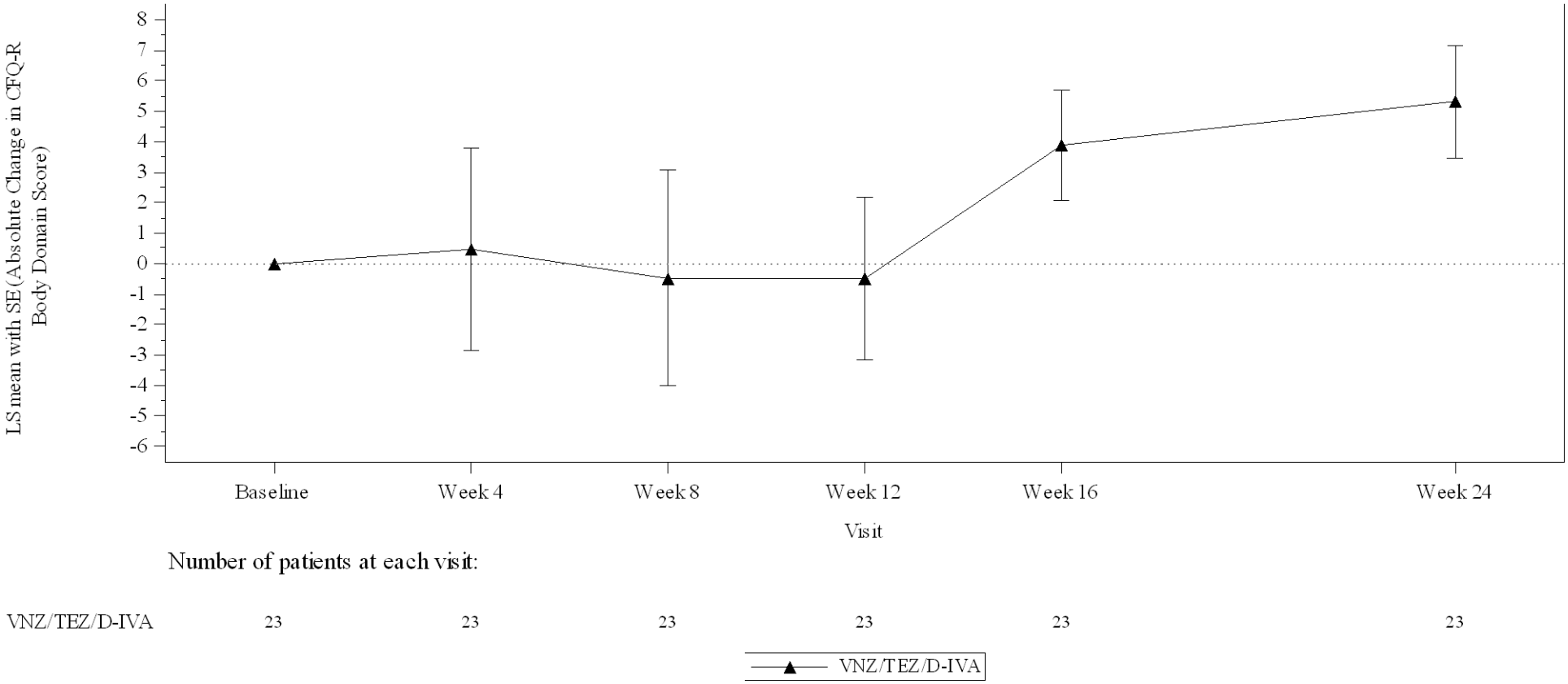
Figure 1.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Respiration



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

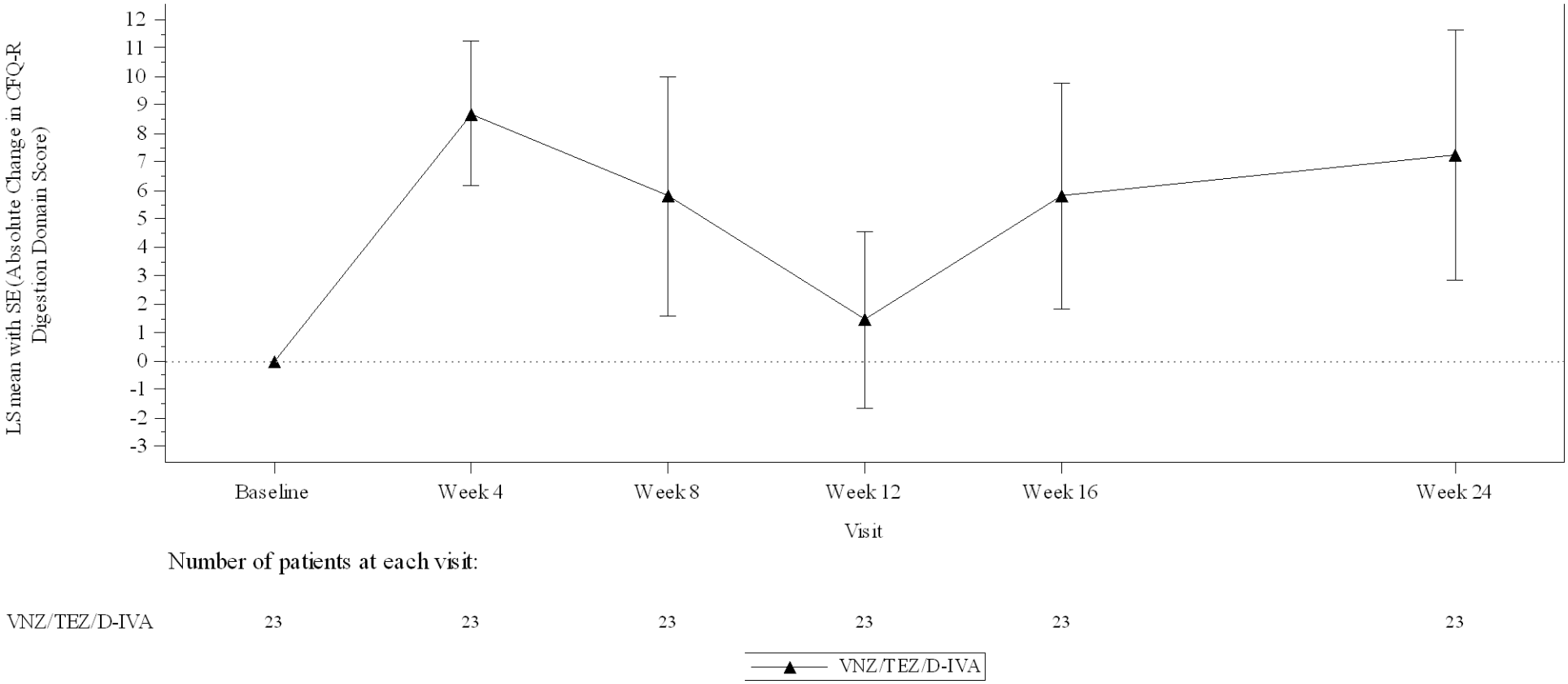
Figure 1.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Body



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

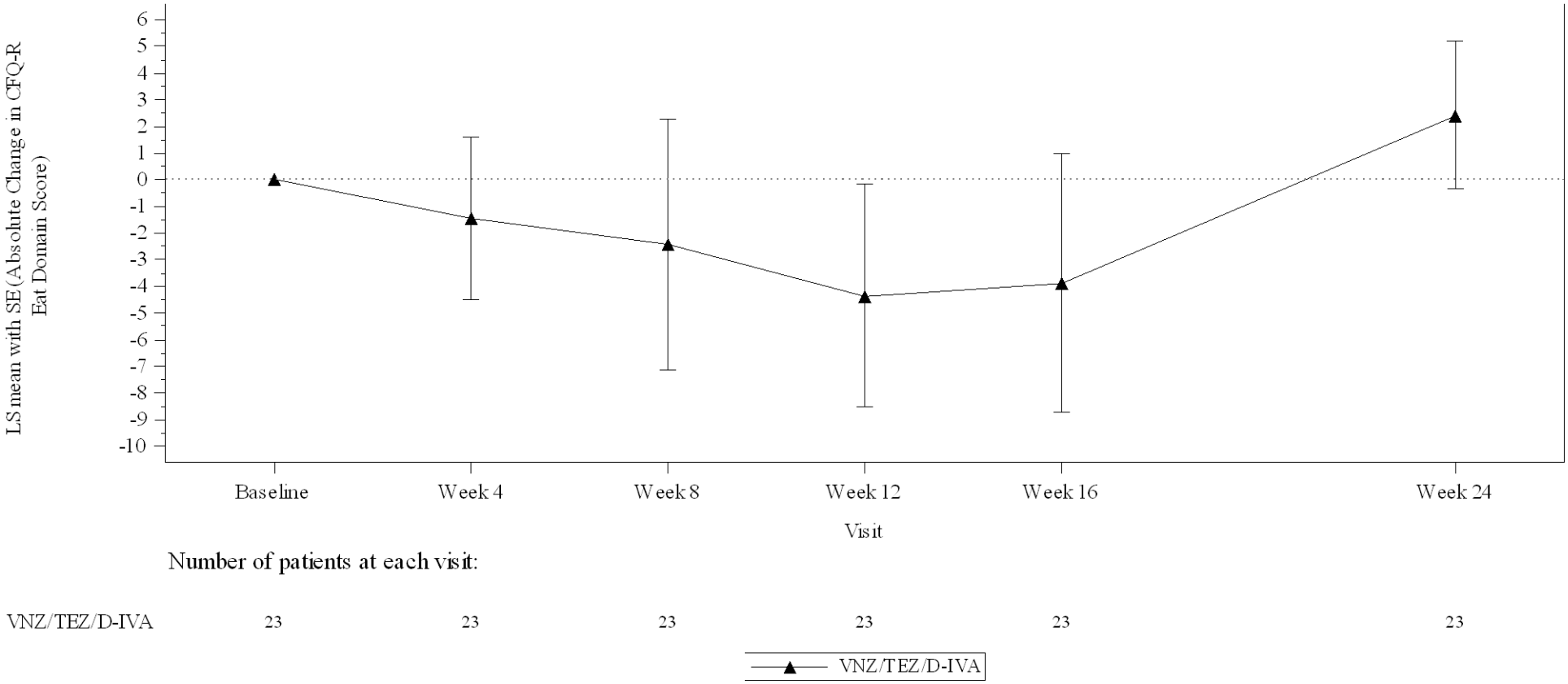
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

Figure 1.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Digestion



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

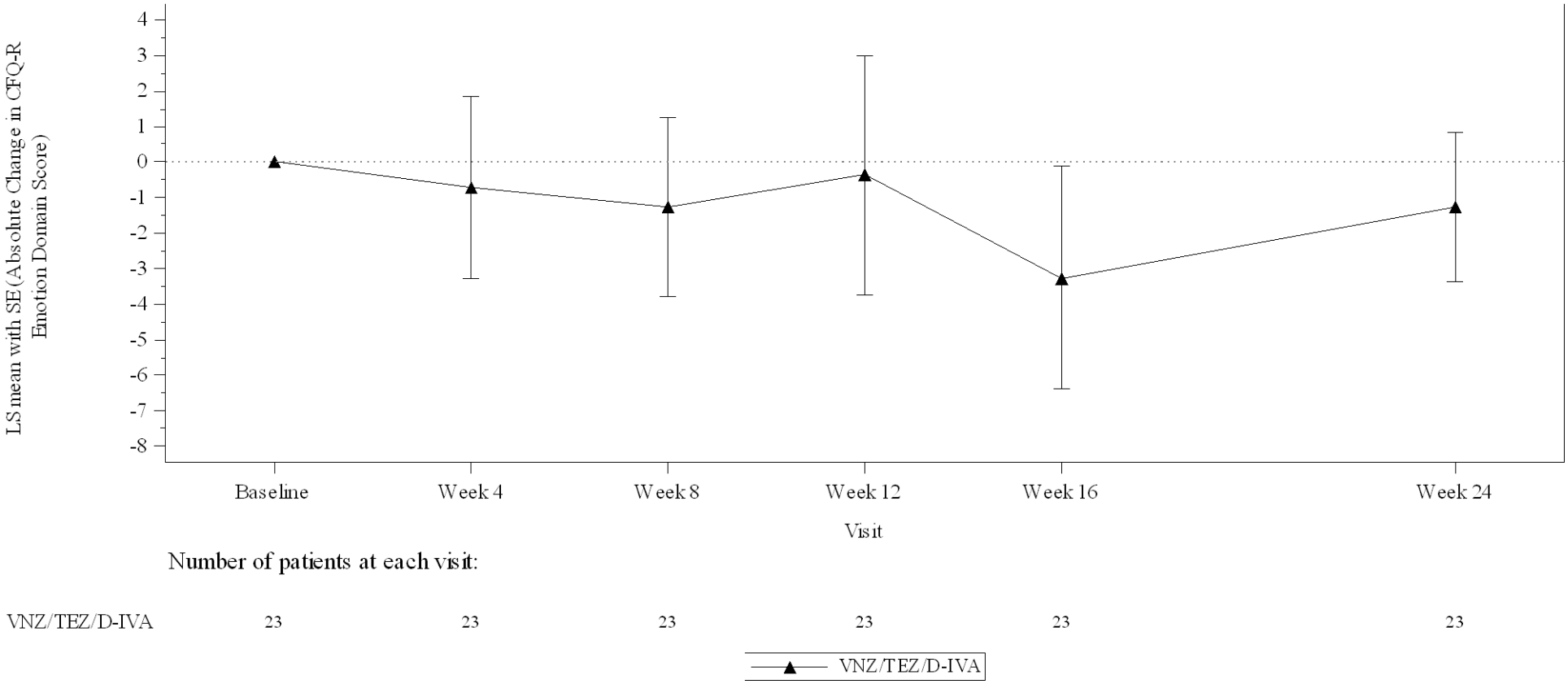
Figure 1.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Eat



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

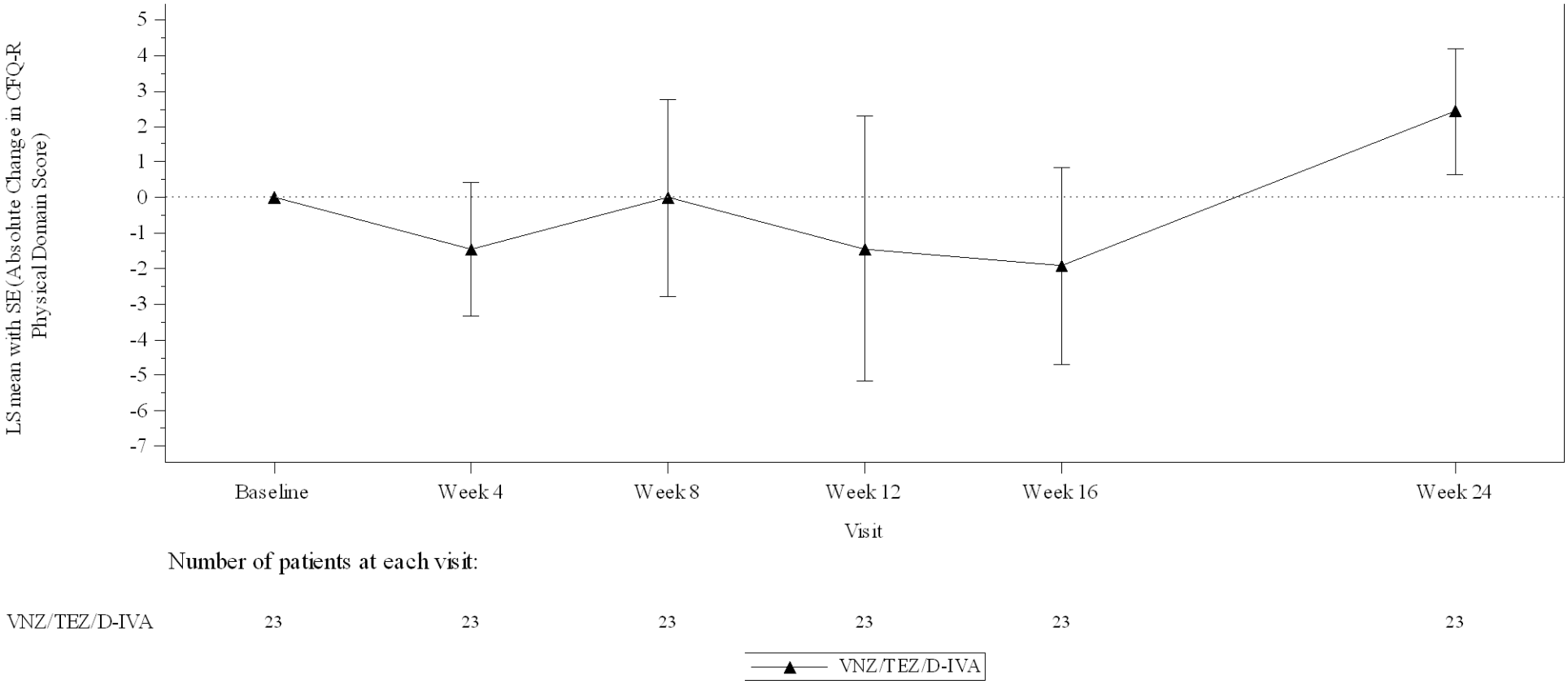
Figure 1.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Emotion



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

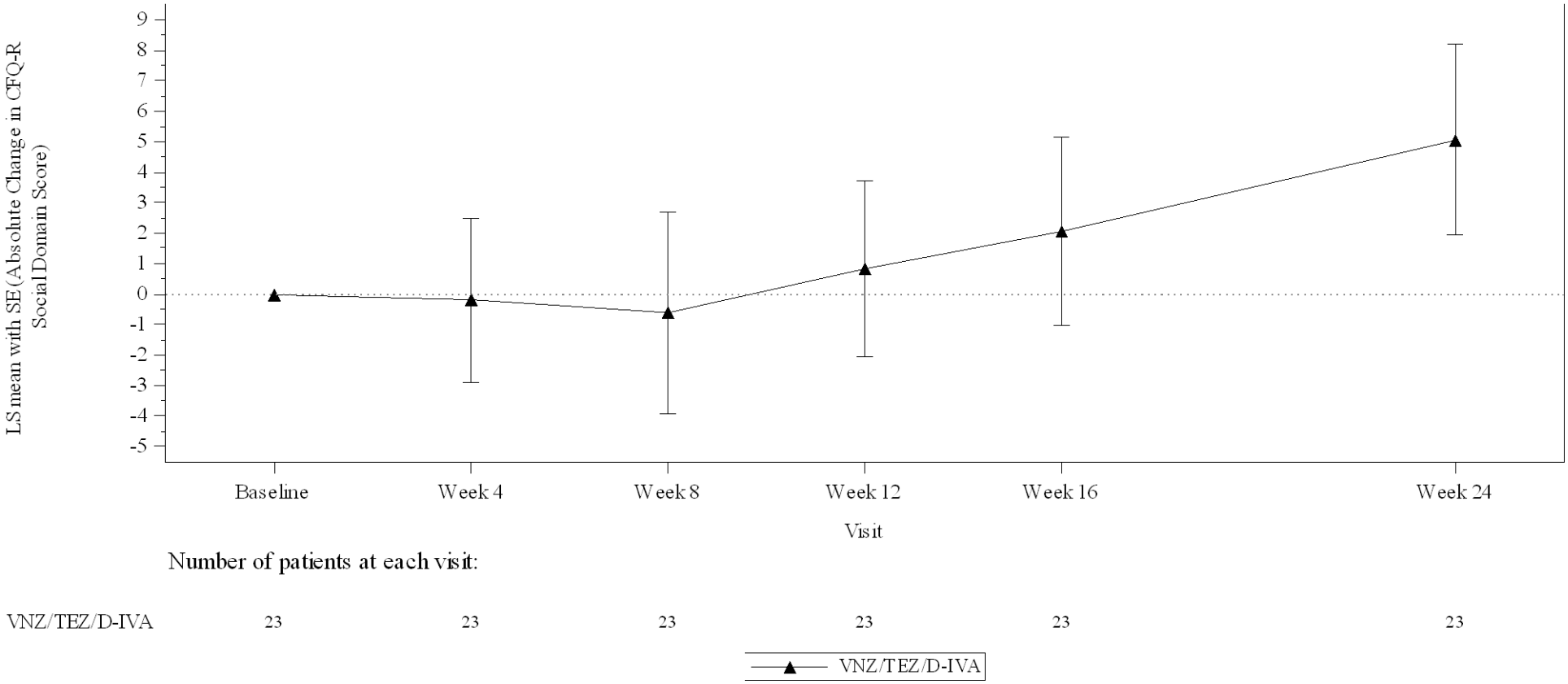
Figure 1.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Physical



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

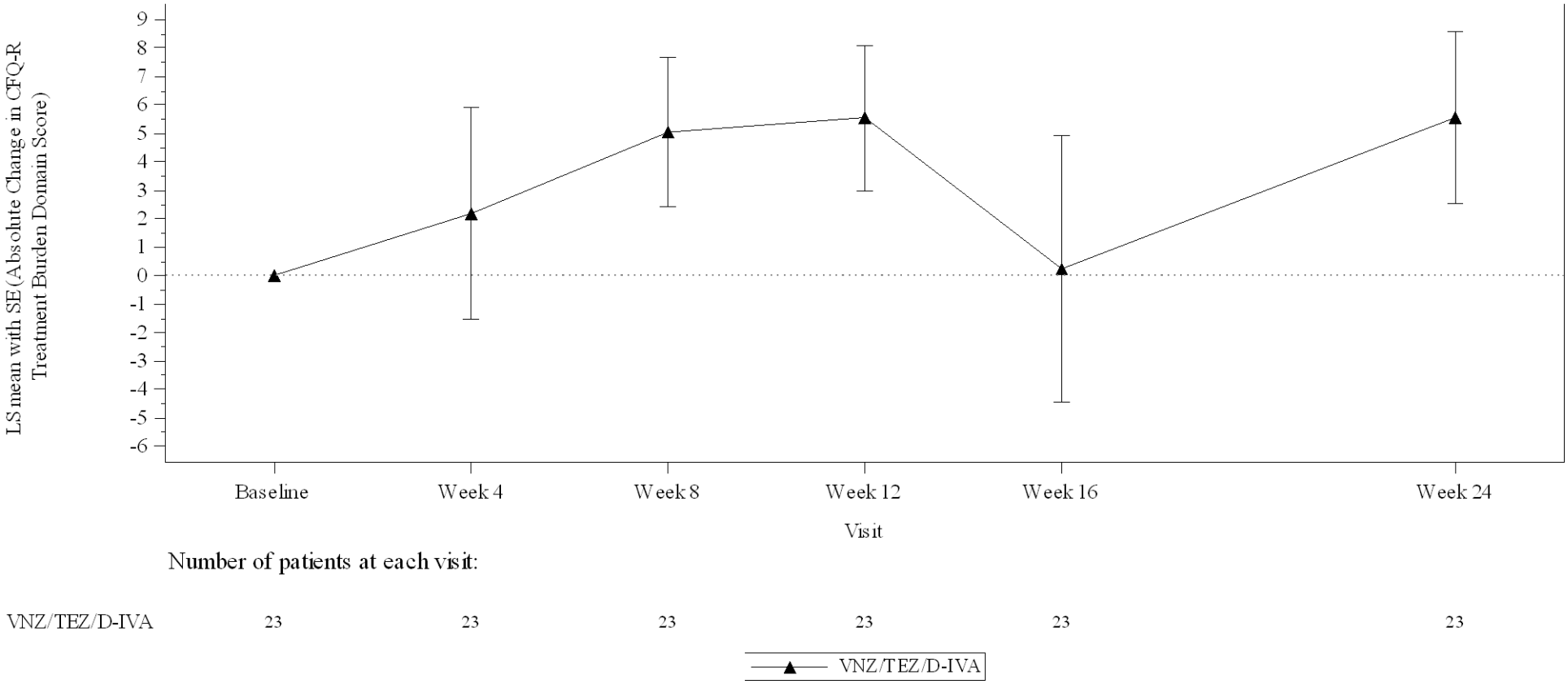
Figure 1.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Social



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

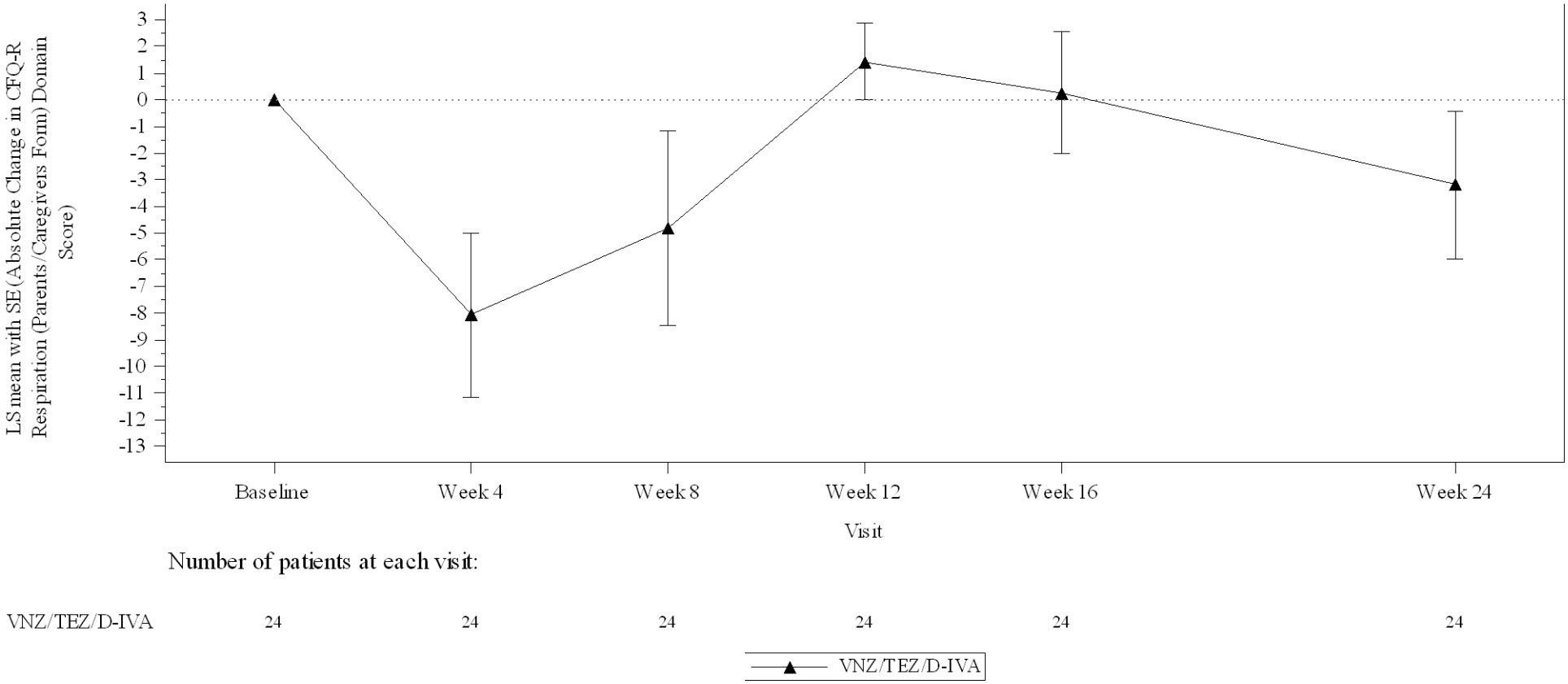
Figure 1.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Treatment Burden



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

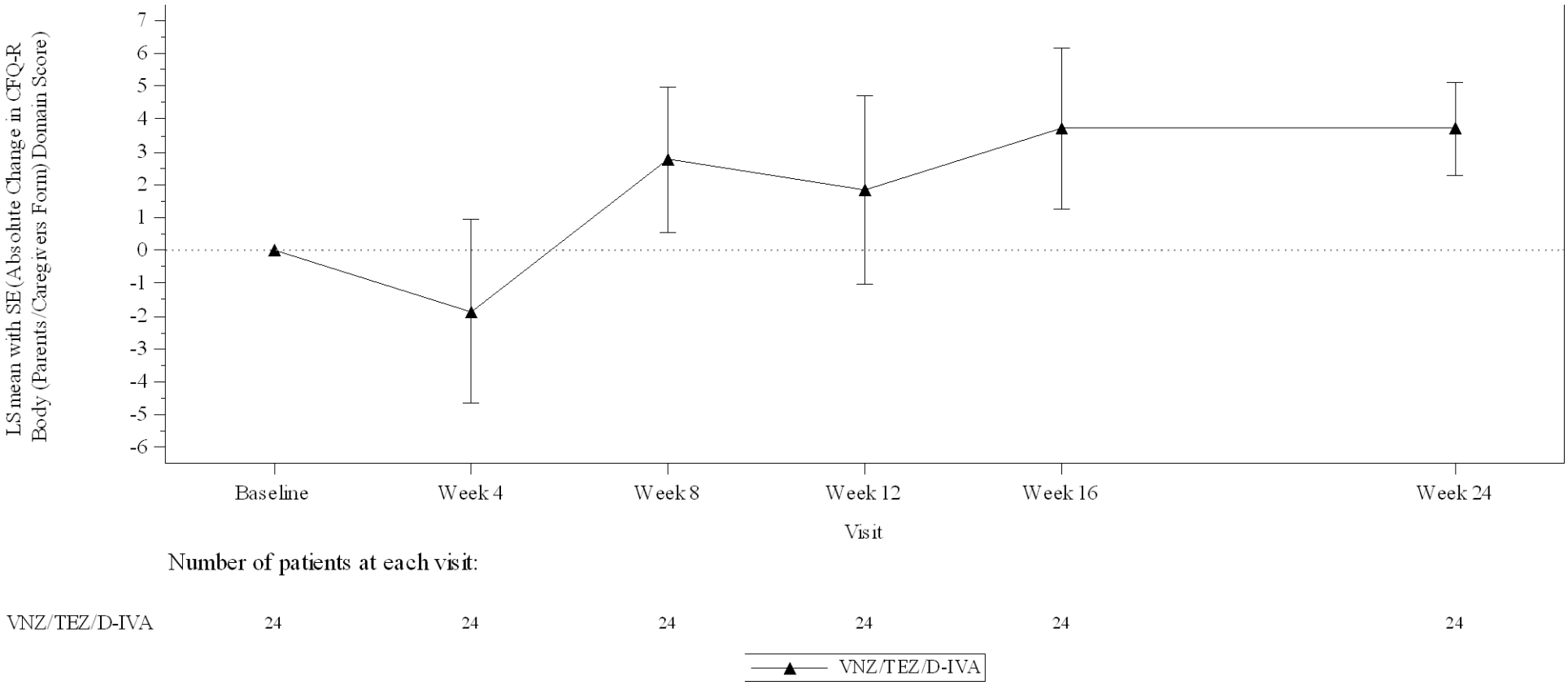
Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

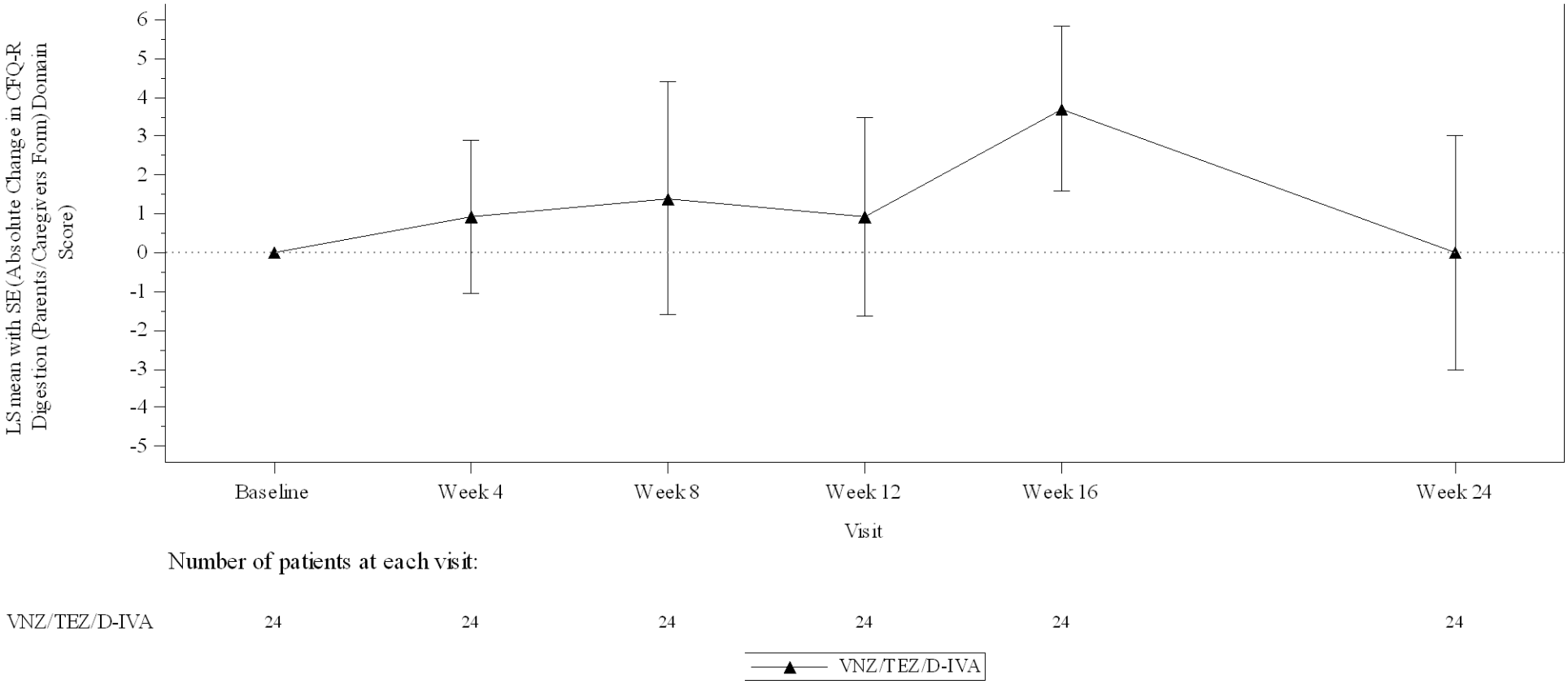
Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Body (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

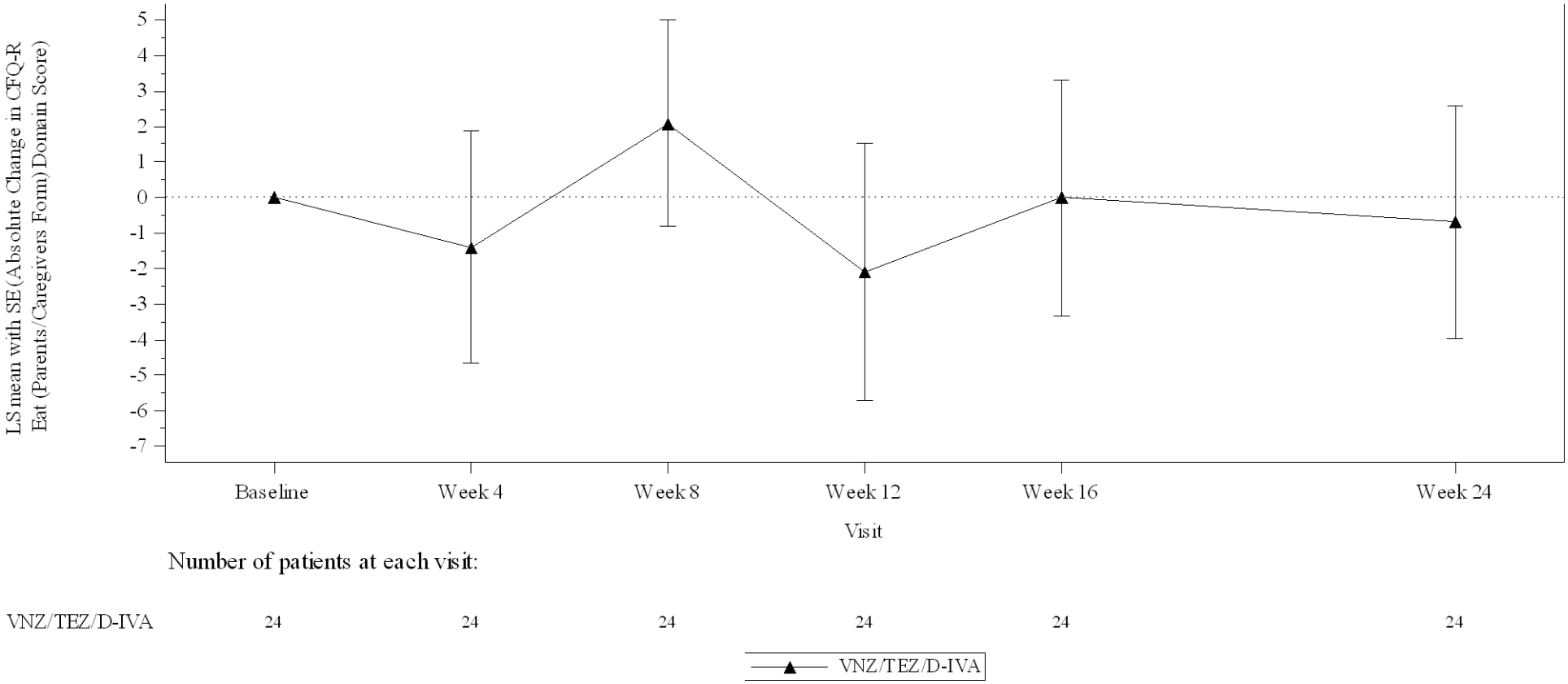
Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

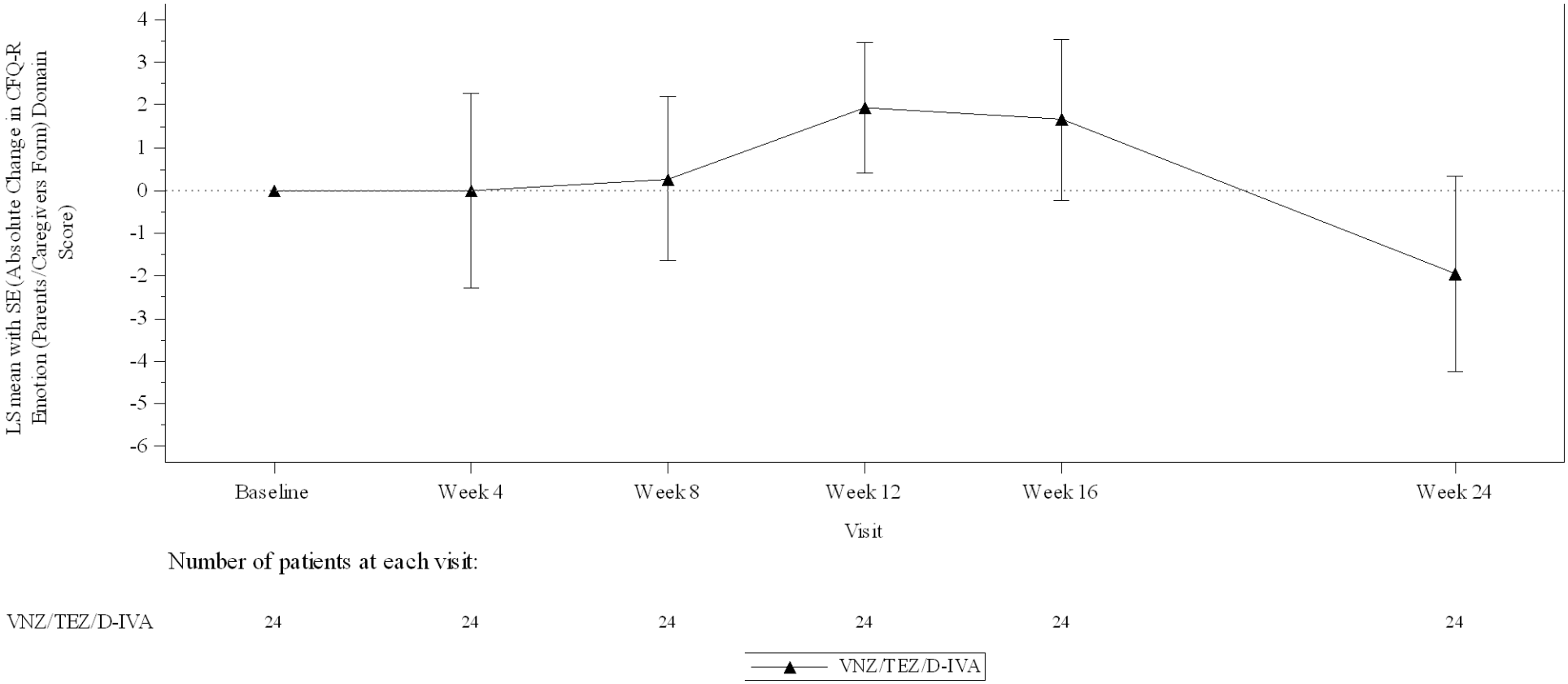
Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

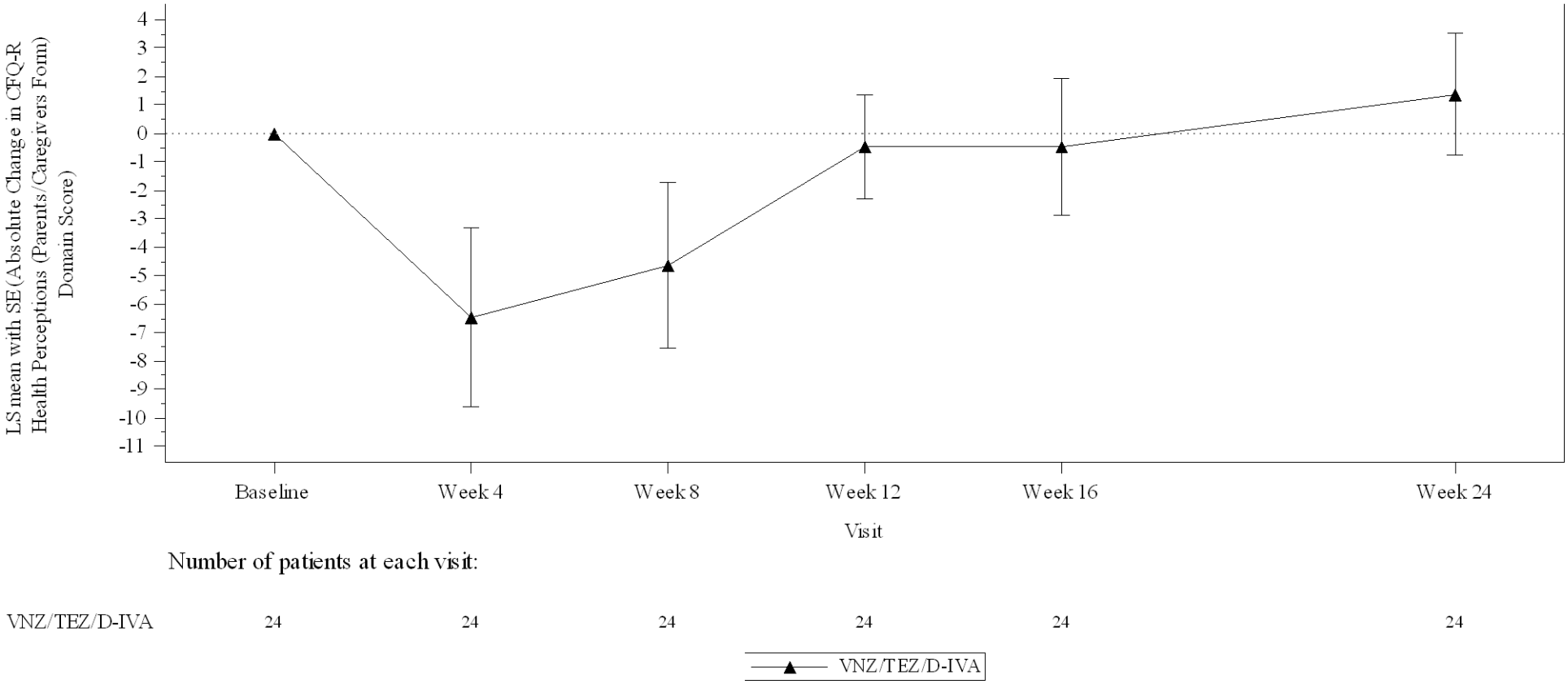
Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

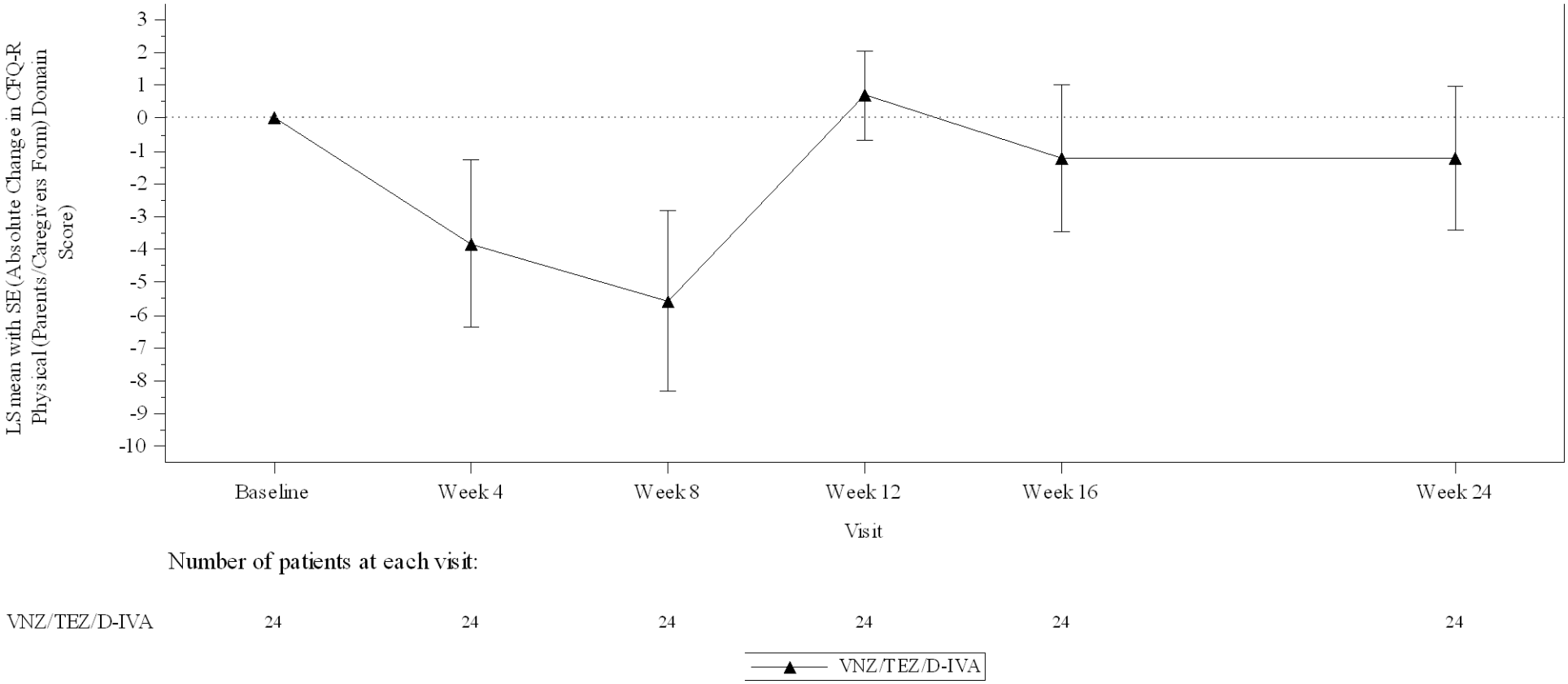
Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

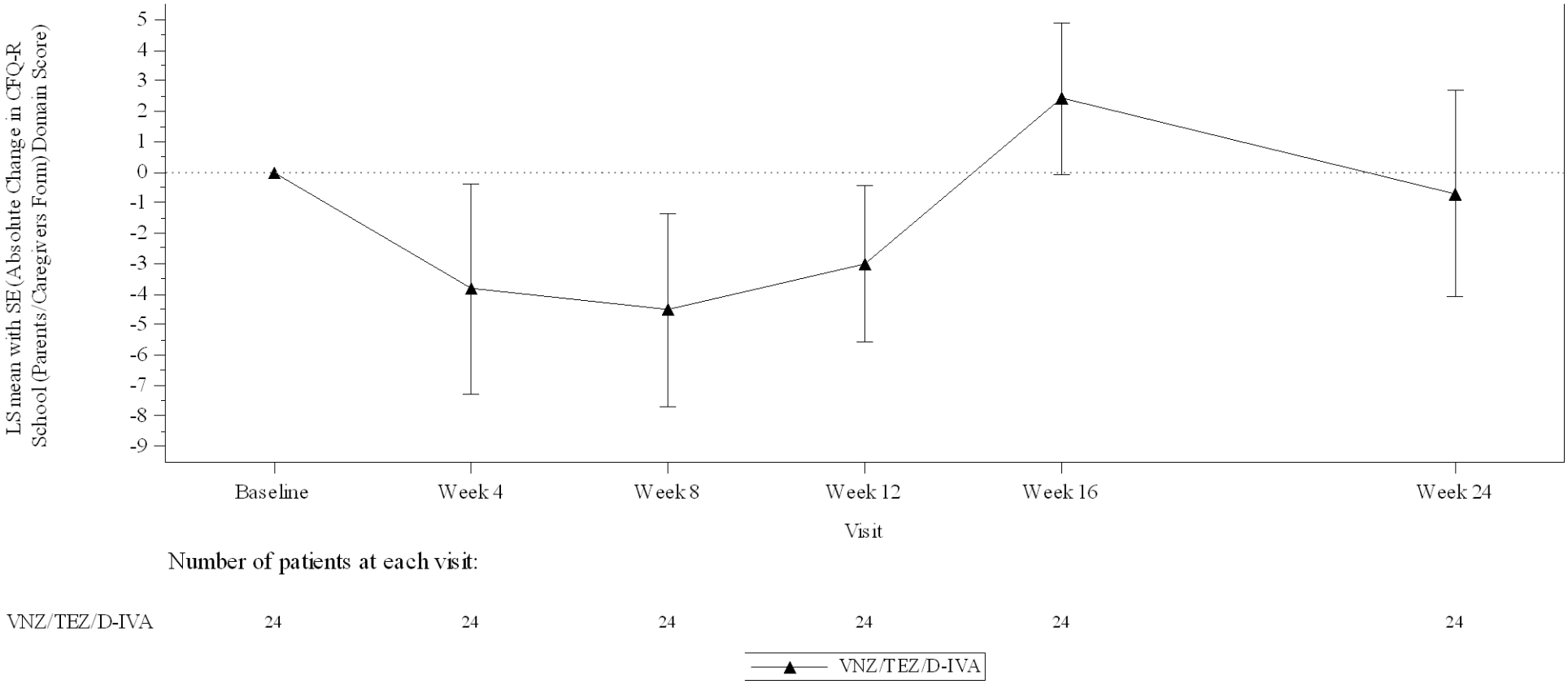
Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

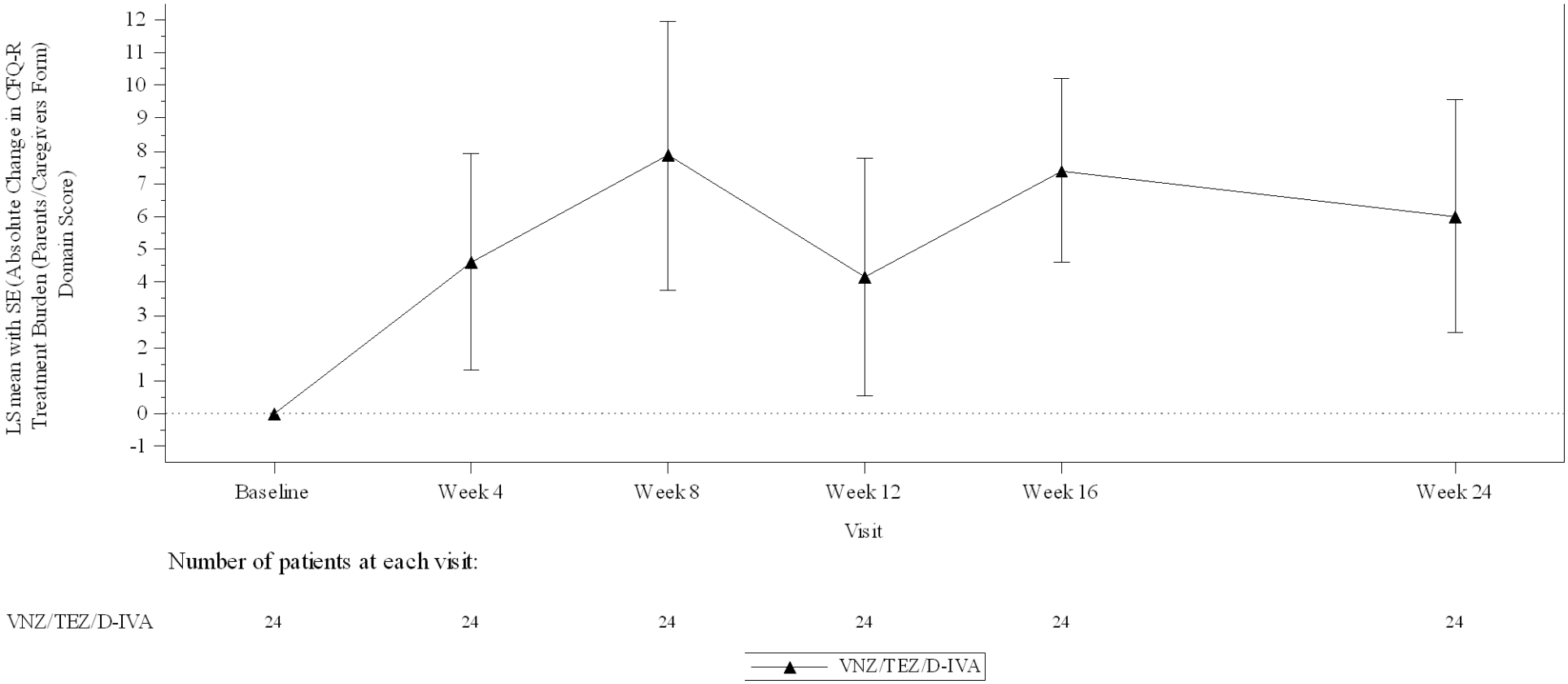
Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: School (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

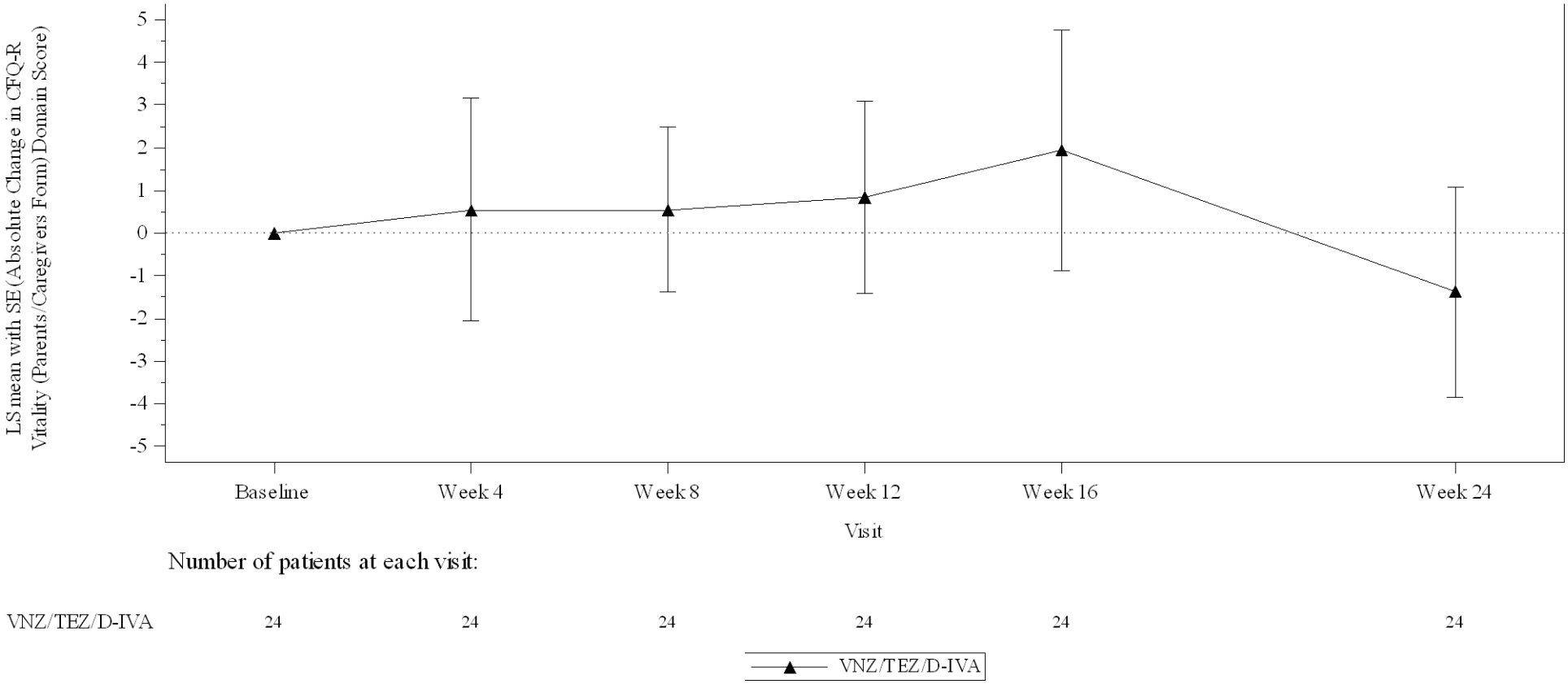
Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

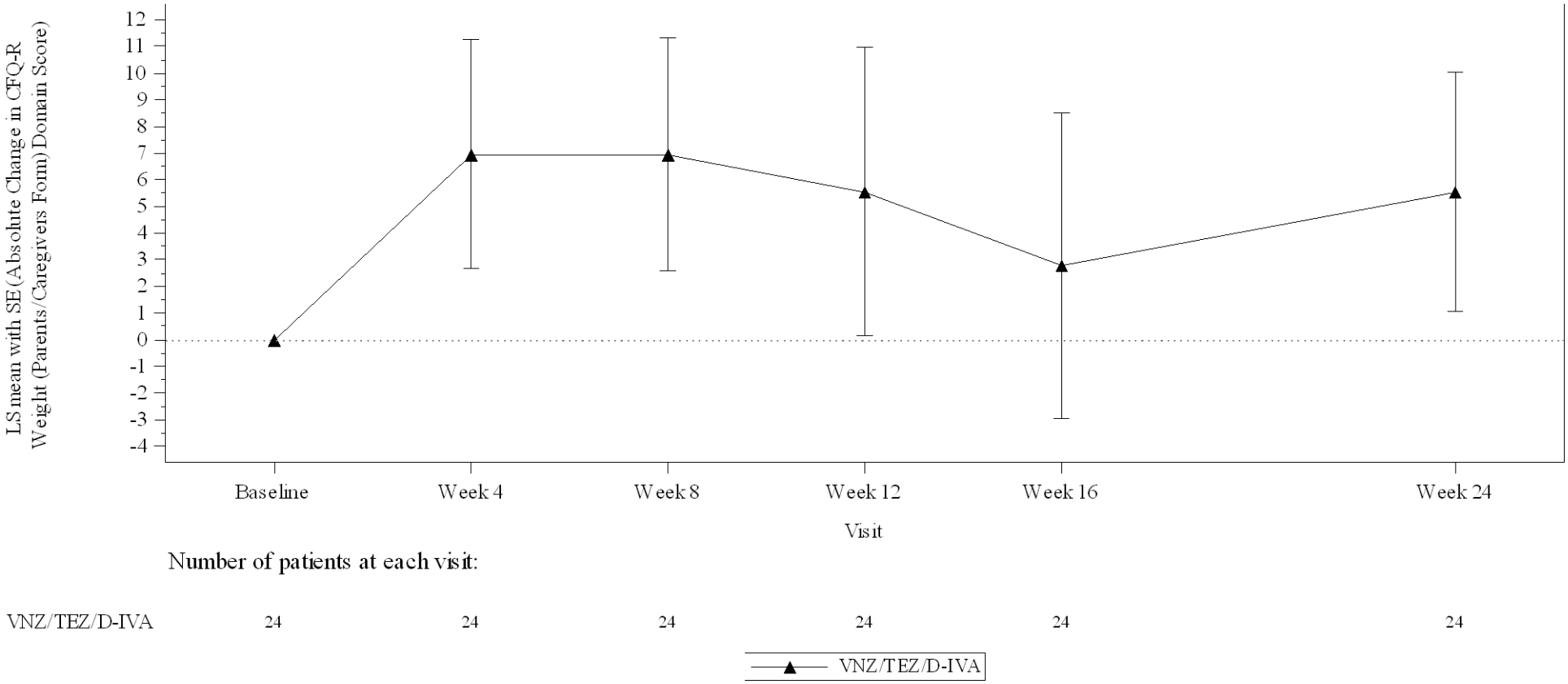
Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

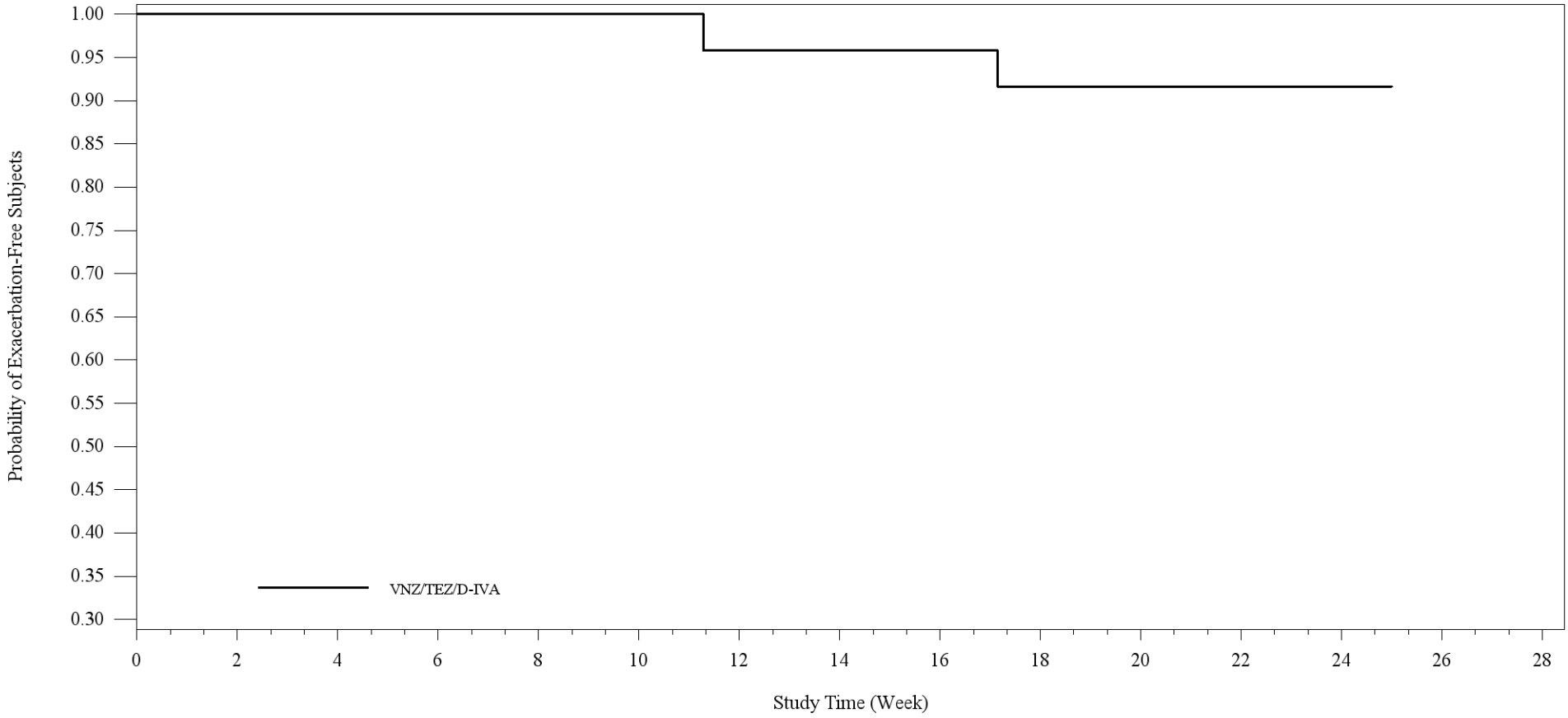
Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

Figure 1.2.1.14.2
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 24 for F/MF
Full Analysis Set

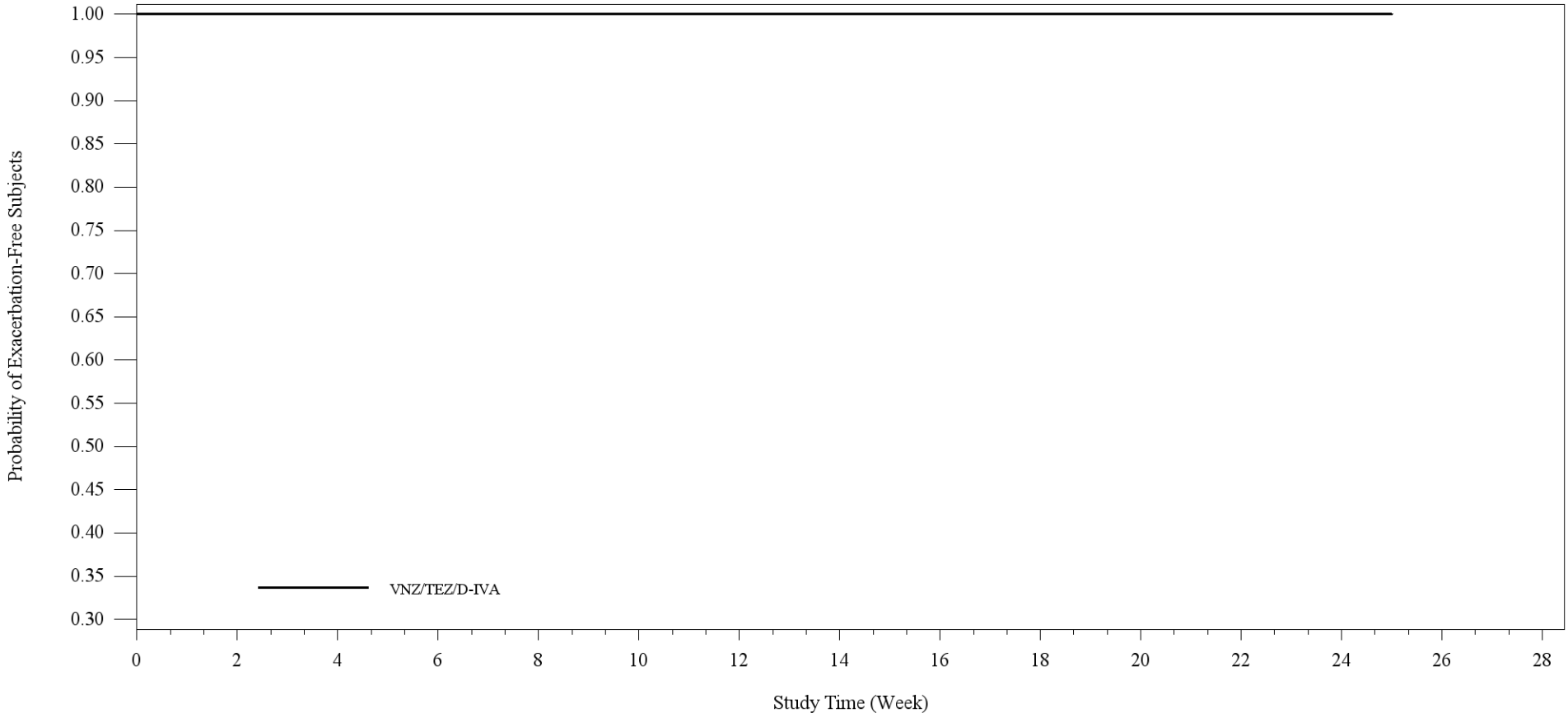


Number of Patients at Risk

VNZ/TEZ/D-IVA	24	24	24	23	23	13

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 1.2.1.15.2
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 24 for F/MF
Full Analysis Set



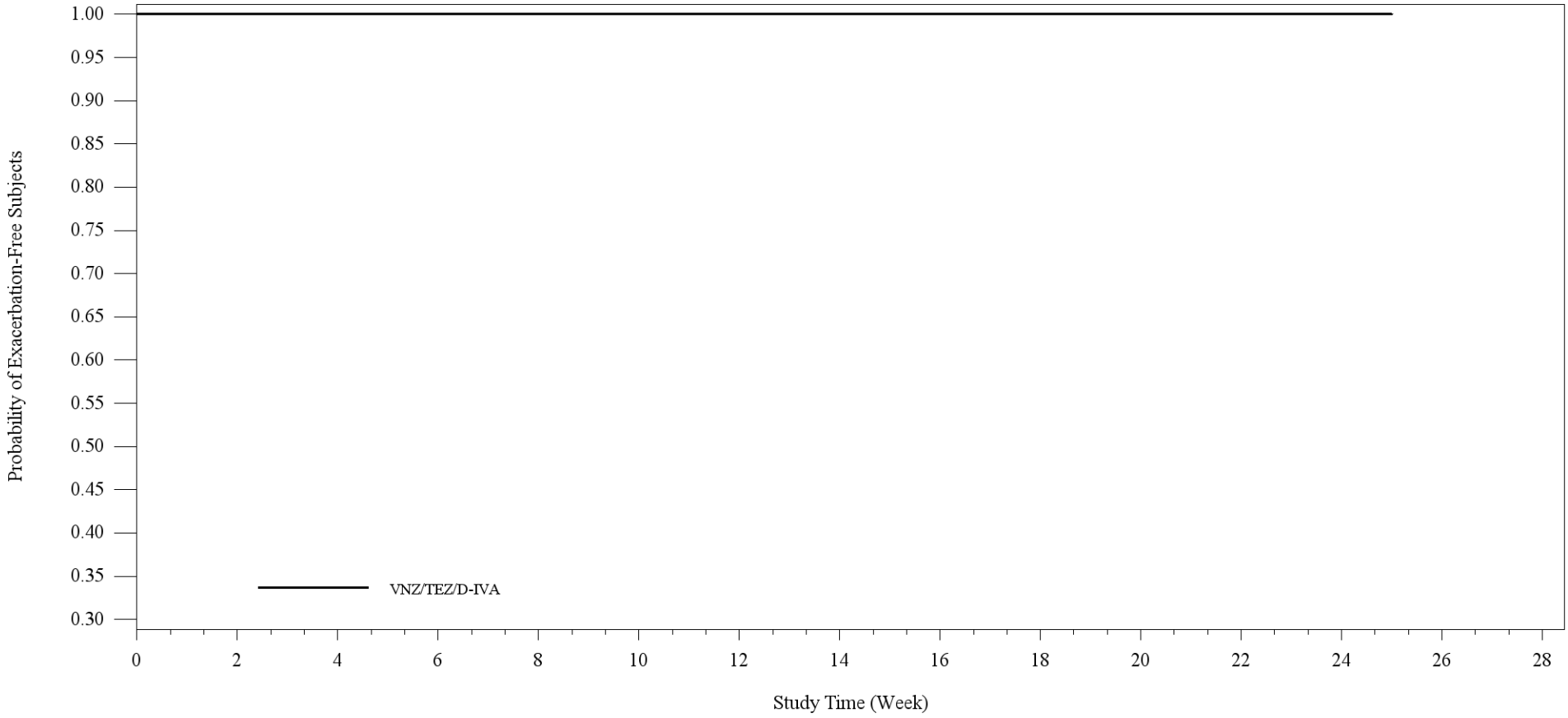
Number of Patients at Risk

VNZ/TEZ/D-IVA	24	24	24	24	24	13

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- The PEx analysis period will include the time from the first dose date of study drug until the last efficacy assessment, which may be collected up to the Week 24 Visit or the earlier of Day 169 and the end of study participation if the subject does not have the Week 24 Visit.

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-hosp-km-24wks-b1-fmf.sas Creation: 06FEB2025 10:14

Figure 1.2.1.16.2
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics through Week 24 for F/MF
Full Analysis Set



Number of Patients at Risk

VNZ/TEZ/D-IVA	24	24	24	24	24	13

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

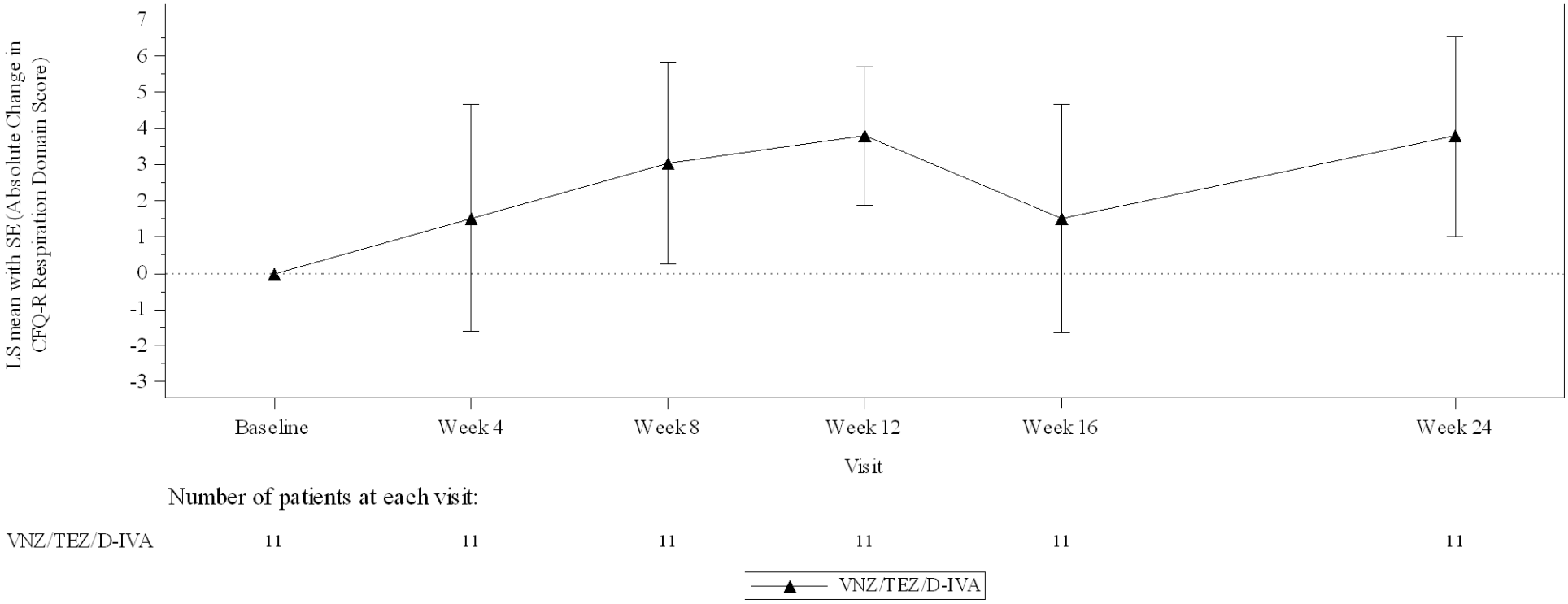
Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

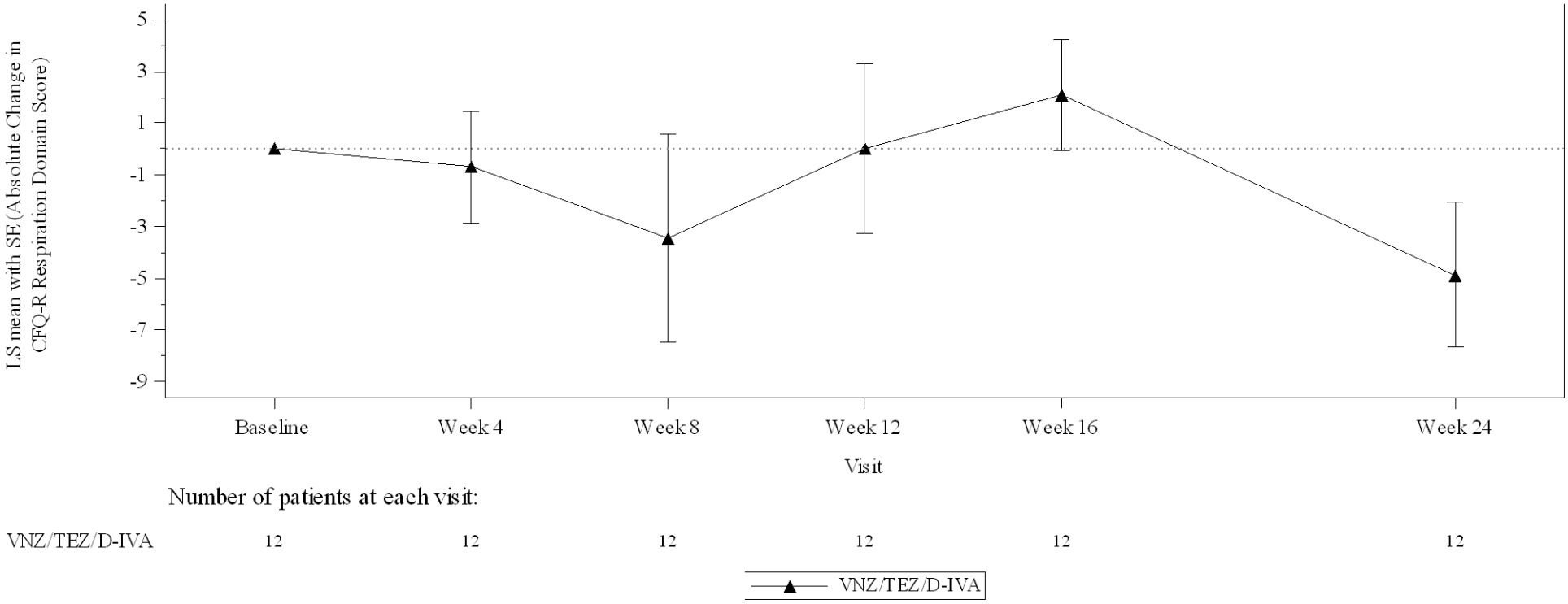
Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body
Sex = Female

Subgroup criteria are not met for this subgroup factor.

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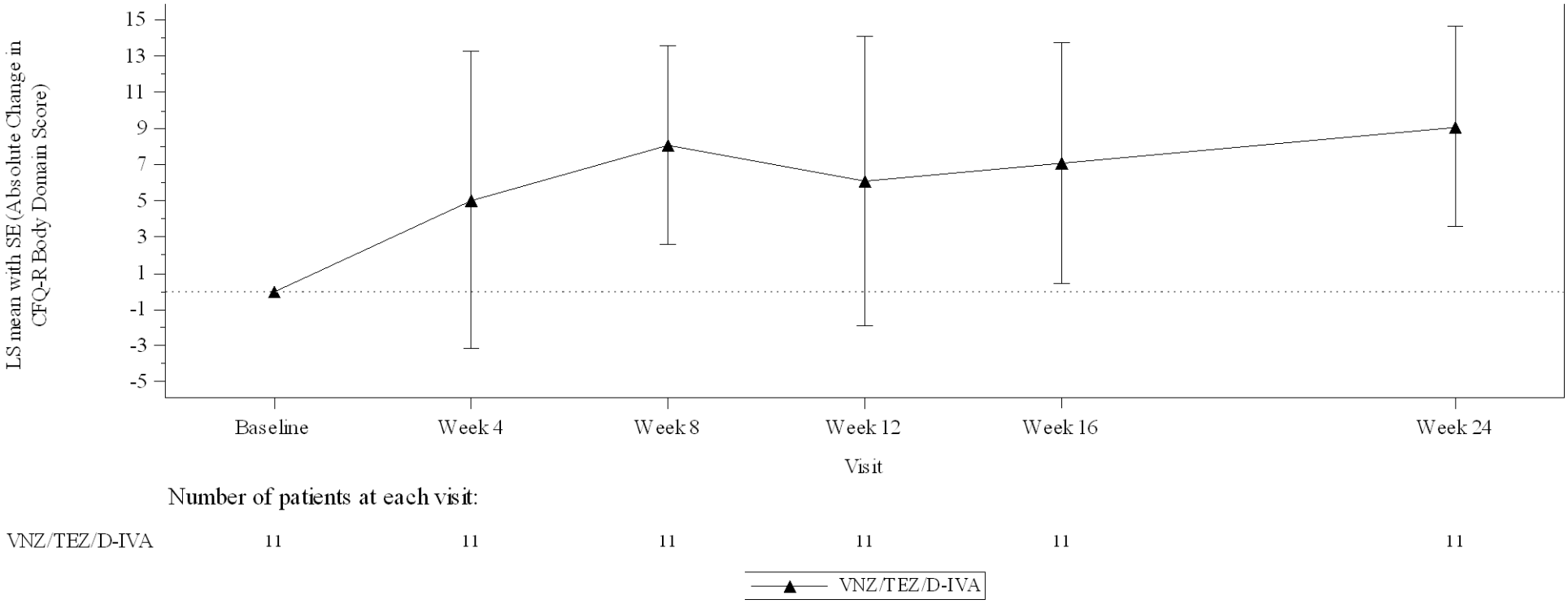
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body
Region = North America



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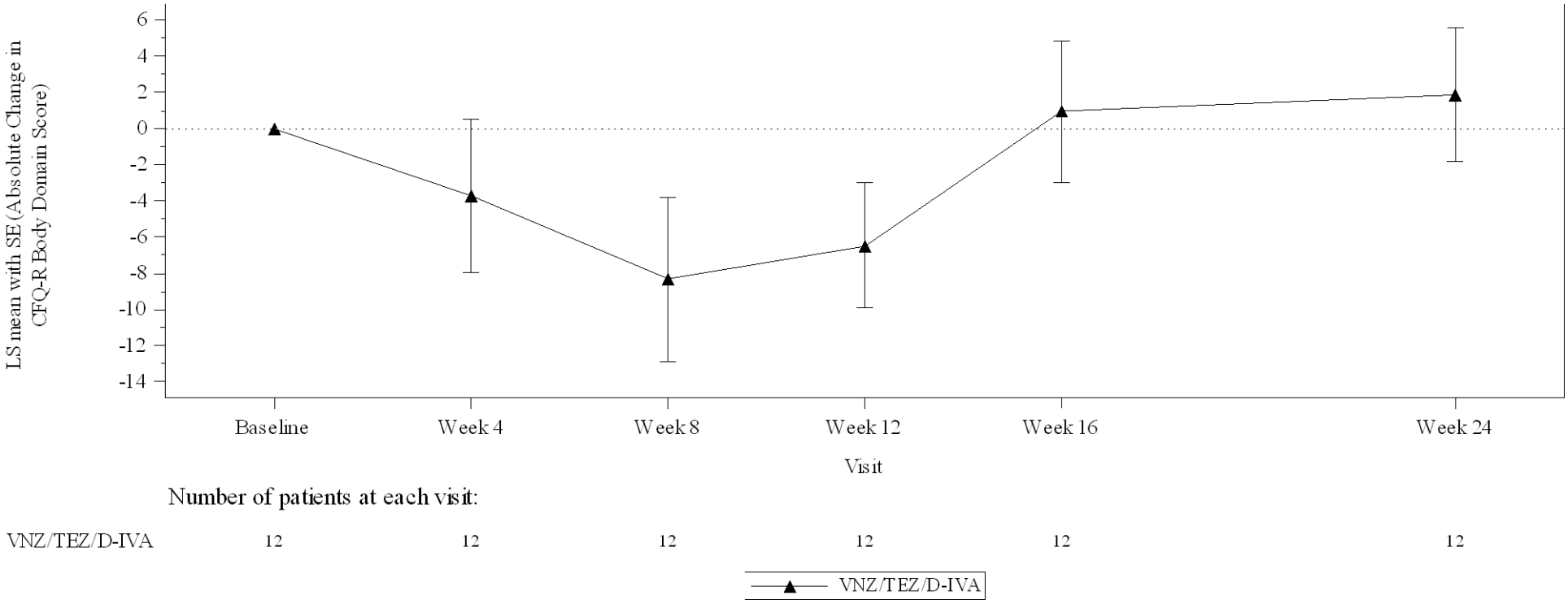
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body
Region = Rest of World



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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion
Sex = Male

Subgroup criteria are not met for this subgroup factor.

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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion
Region = North America

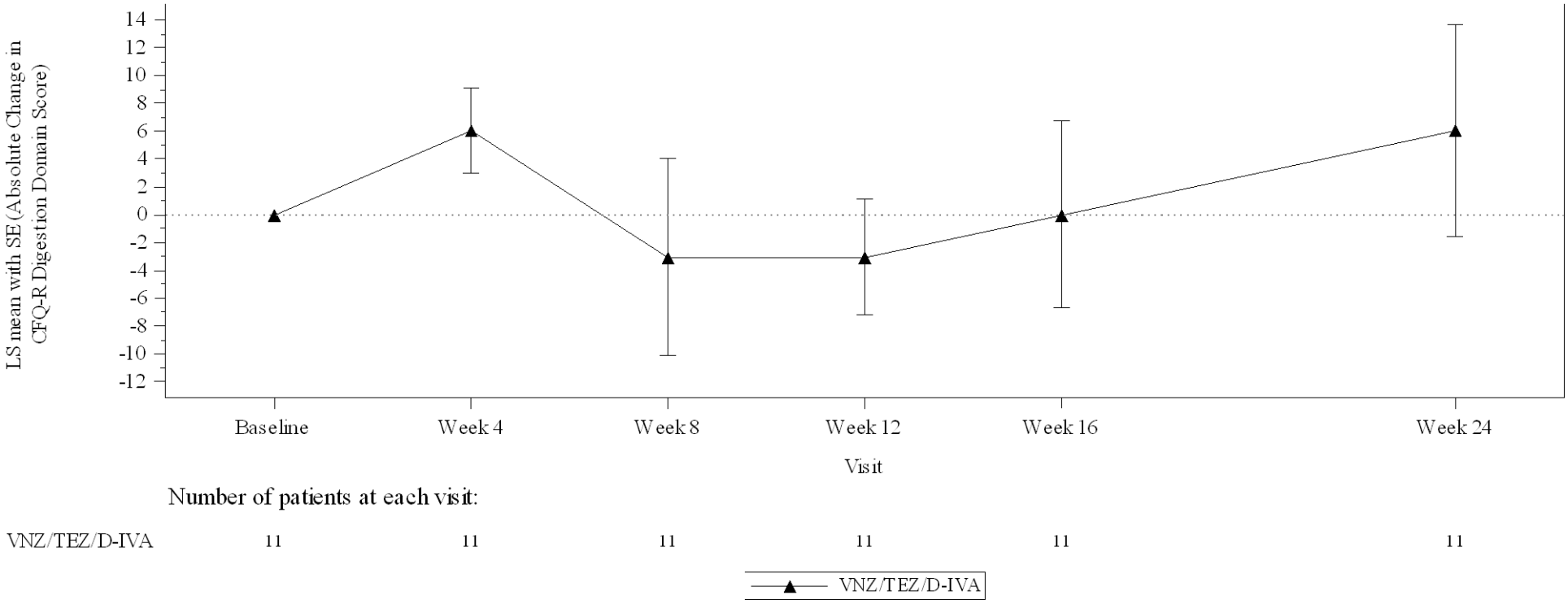

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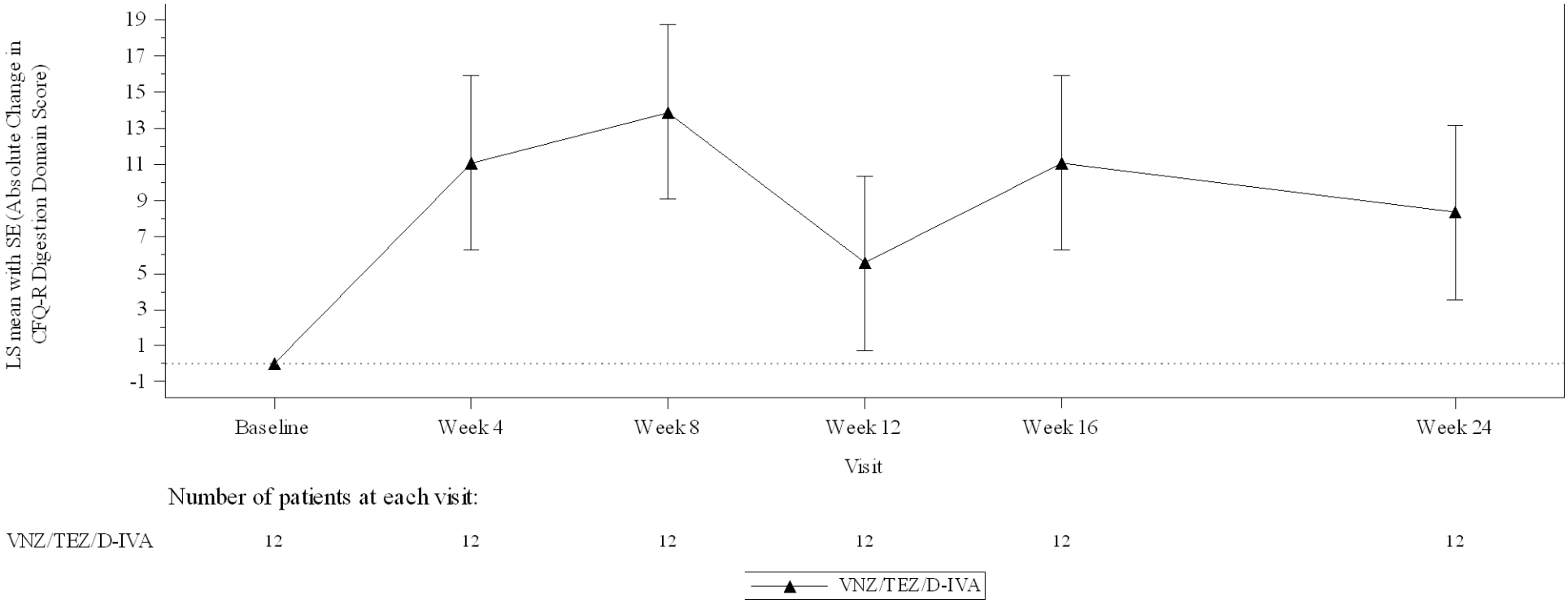
Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion
Region = Rest of World



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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

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Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat
Sex = Male

Subgroup criteria are not met for this subgroup factor.

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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat
Sex = Female

Subgroup criteria are not met for this subgroup factor.

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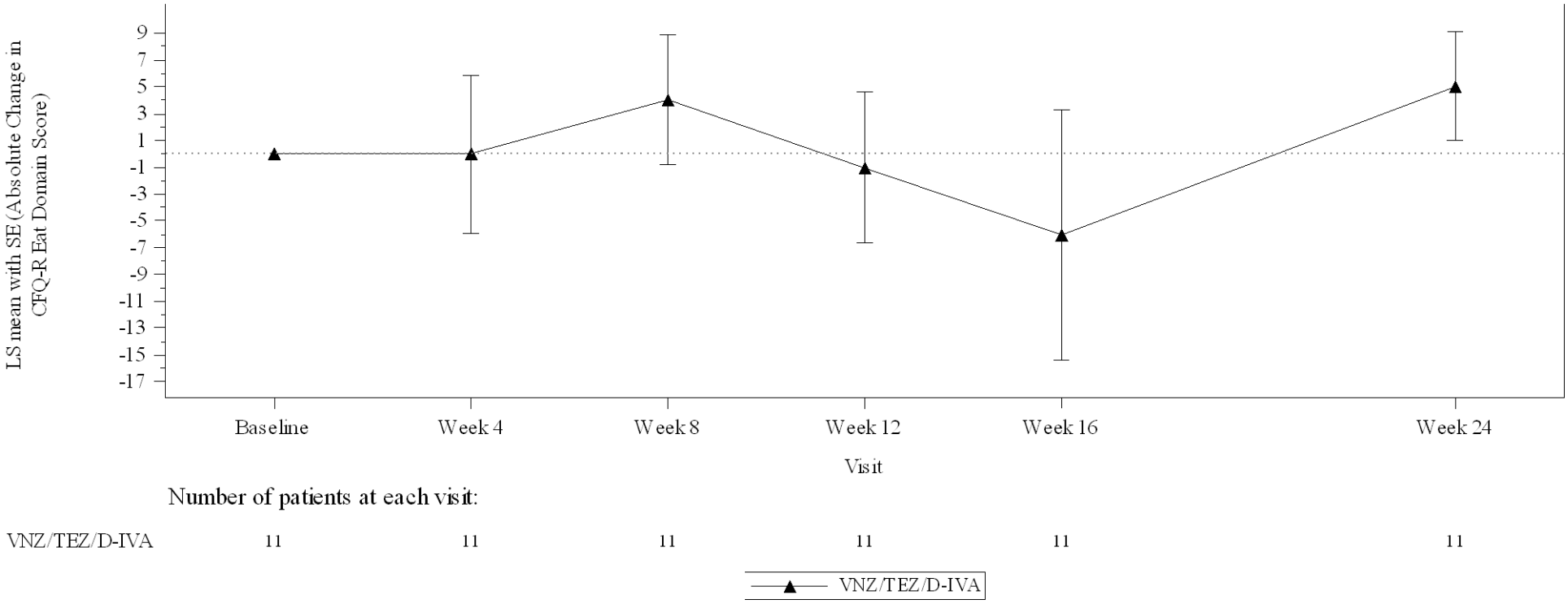
Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat
Region = North America



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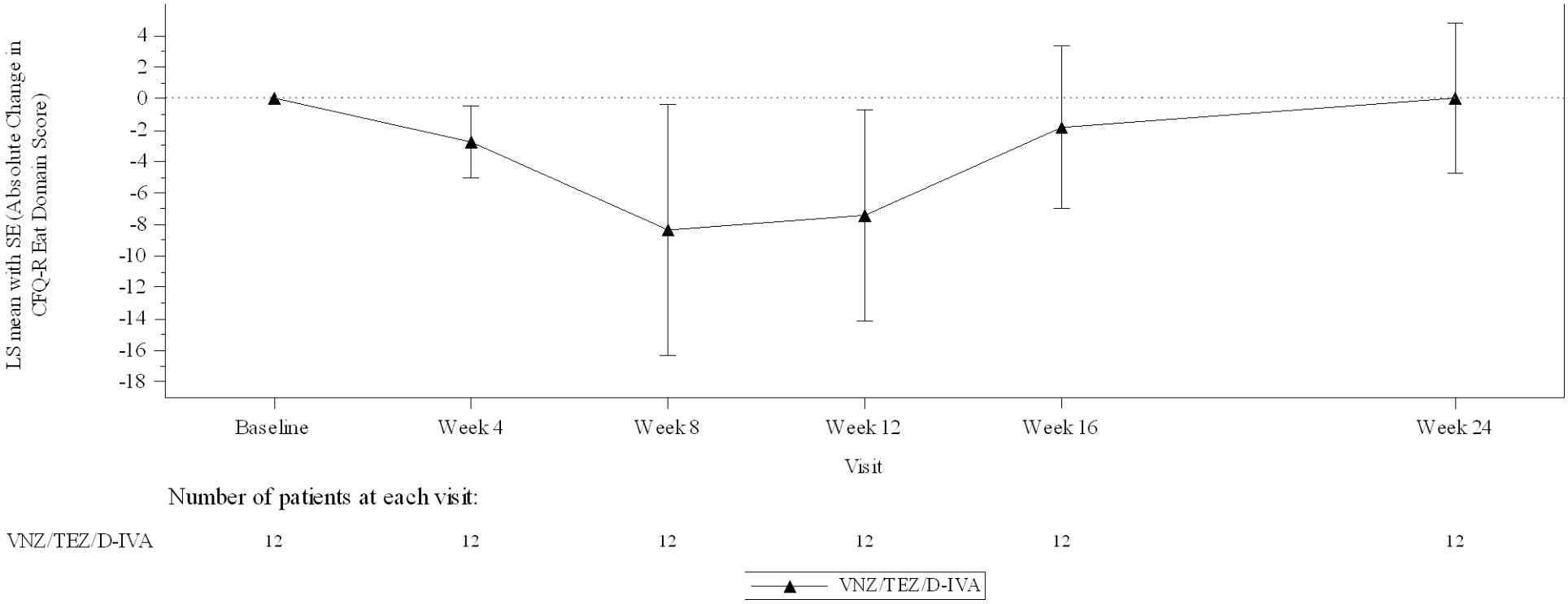
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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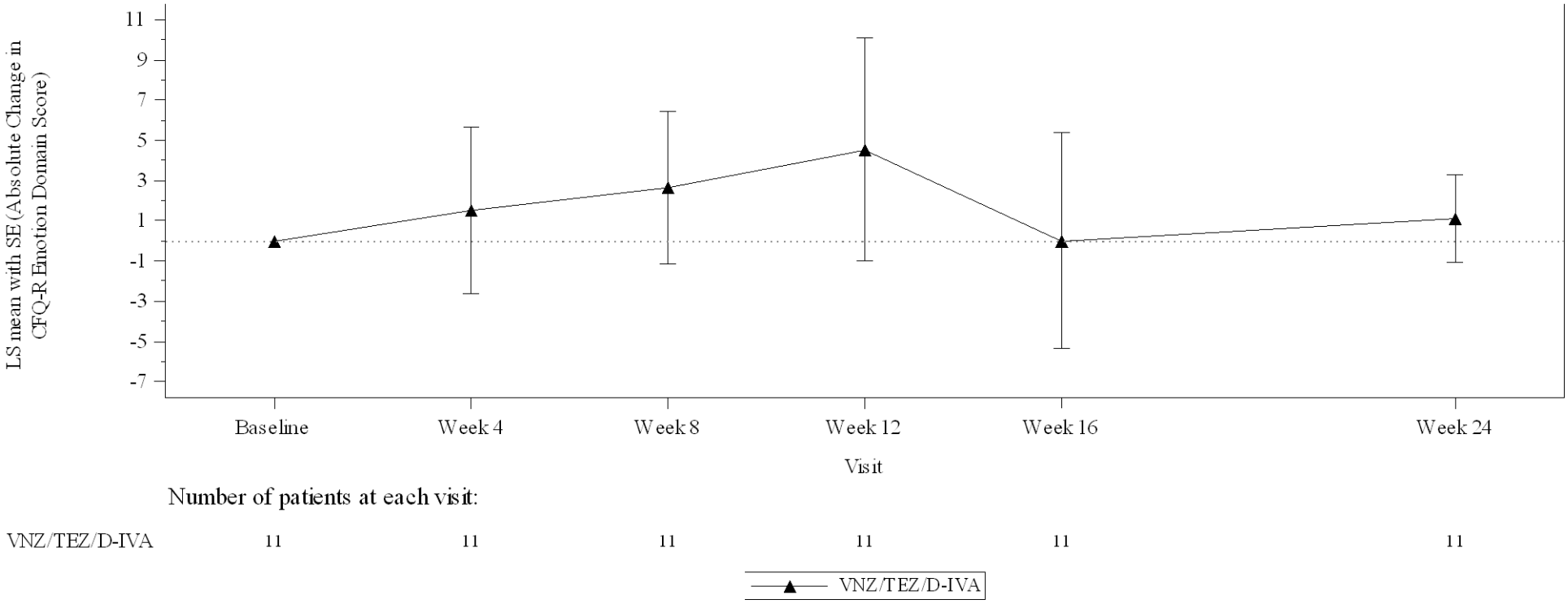
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion
Region = North America



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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion
Region = Rest of World

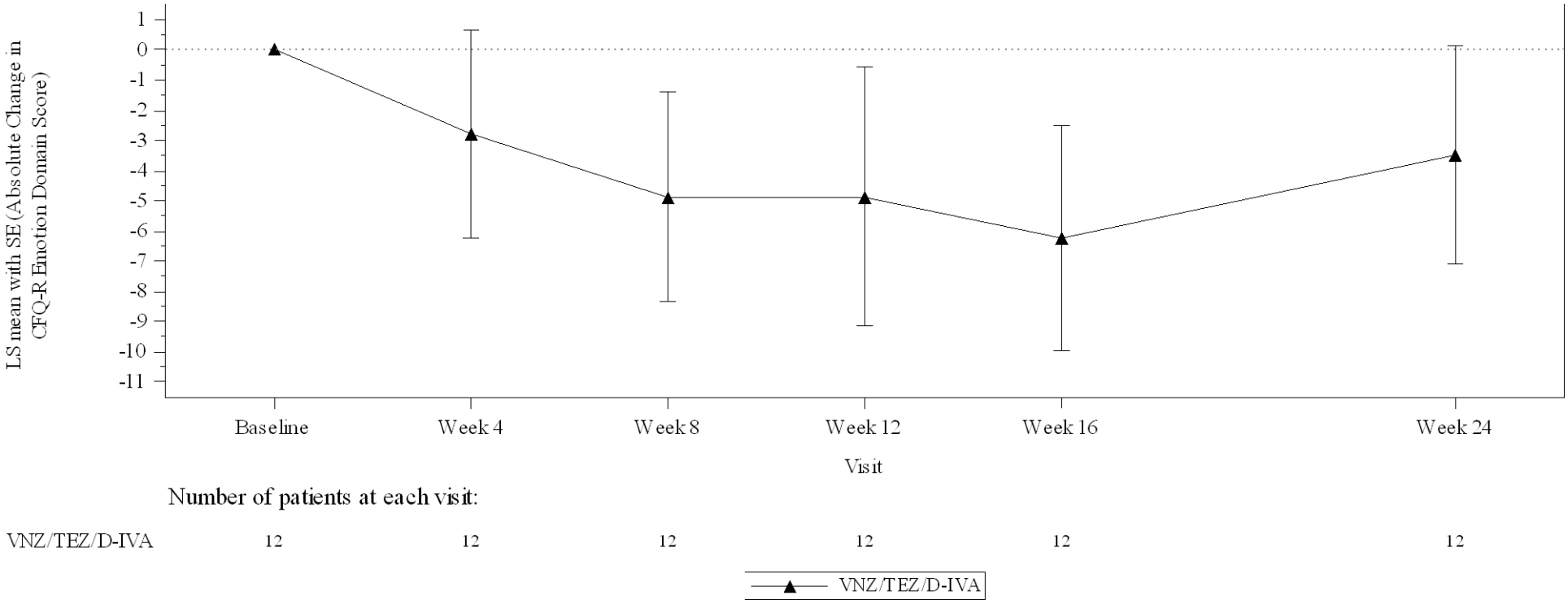

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Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

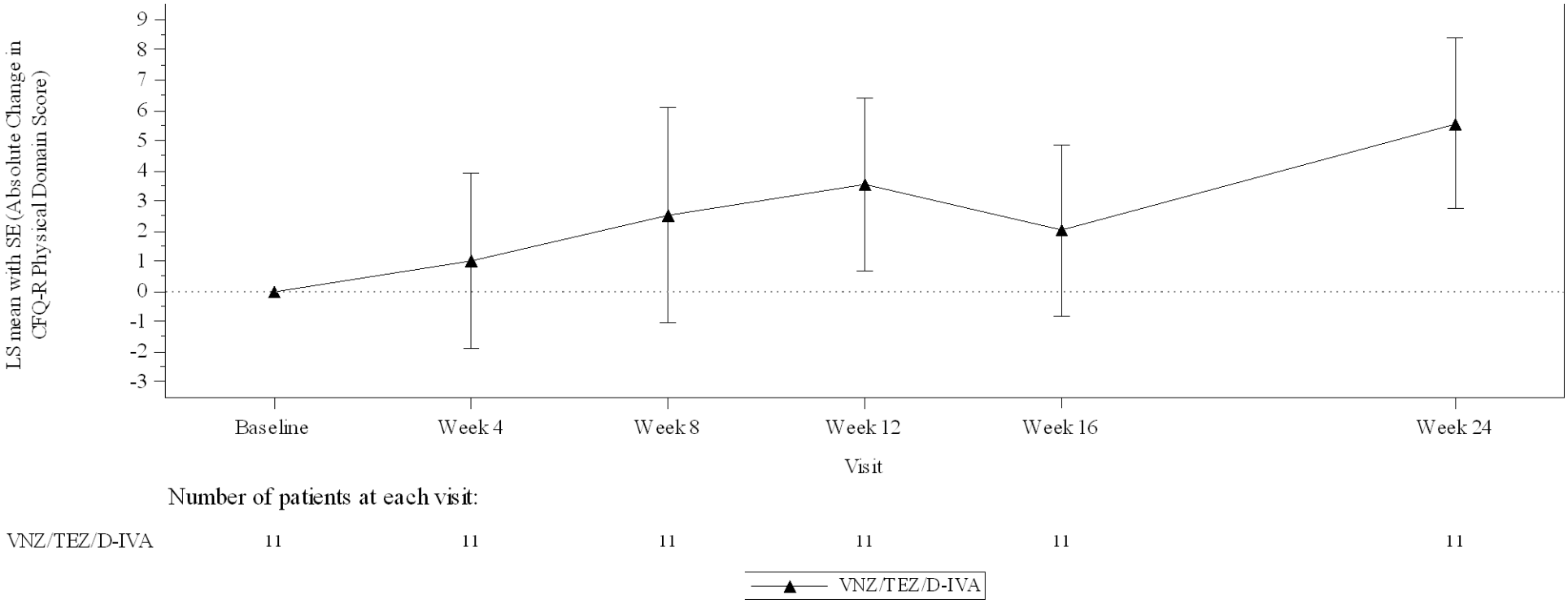
Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

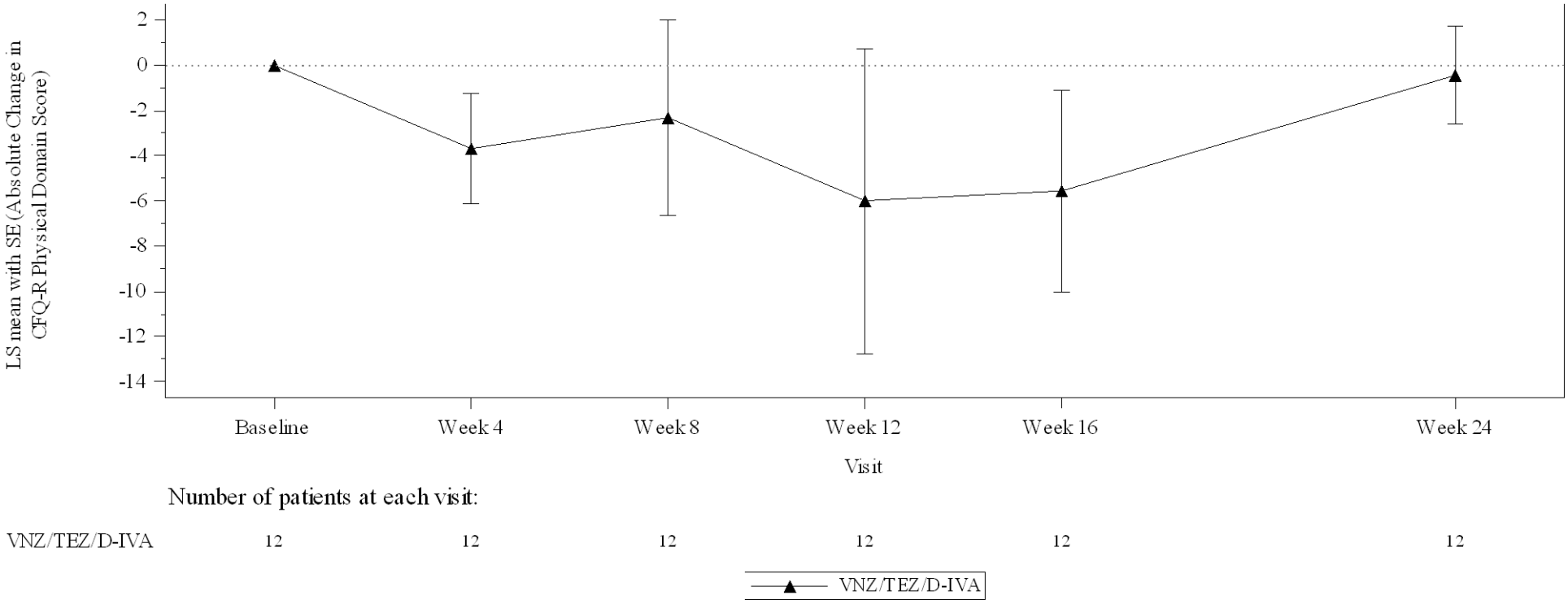
Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Social
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

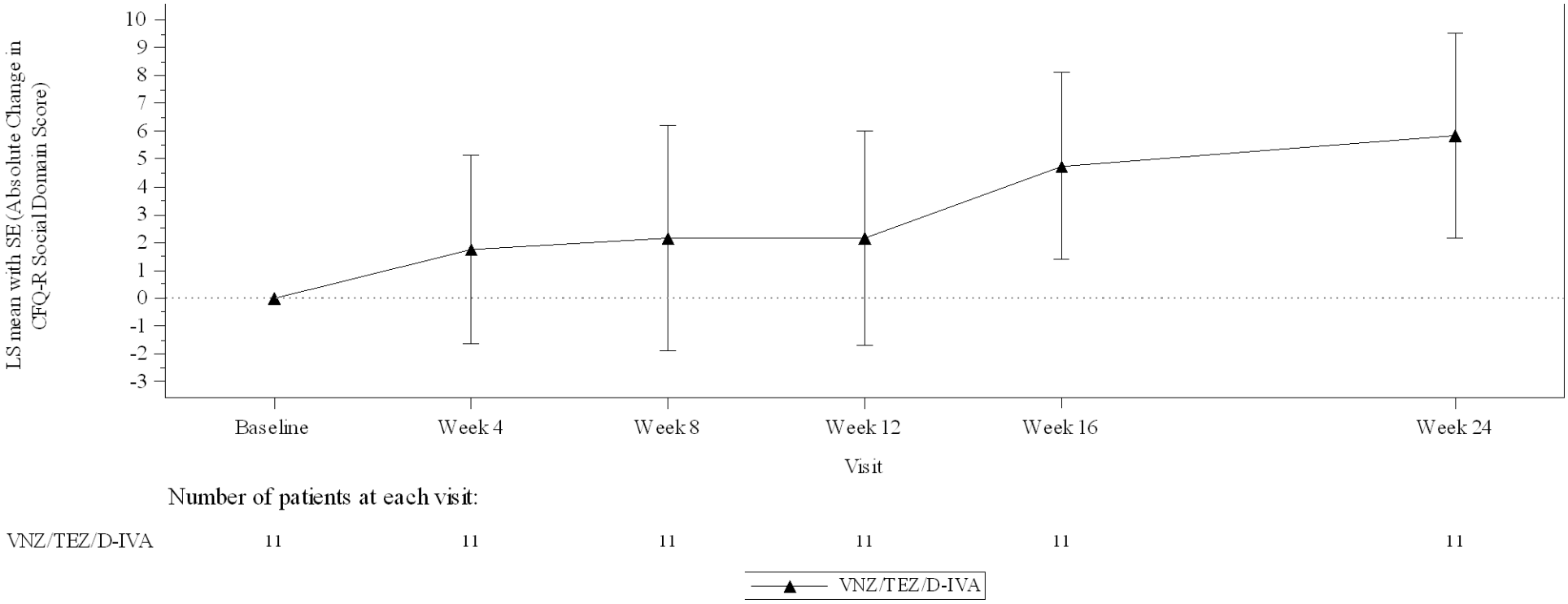
Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Social
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Social
Region = North America



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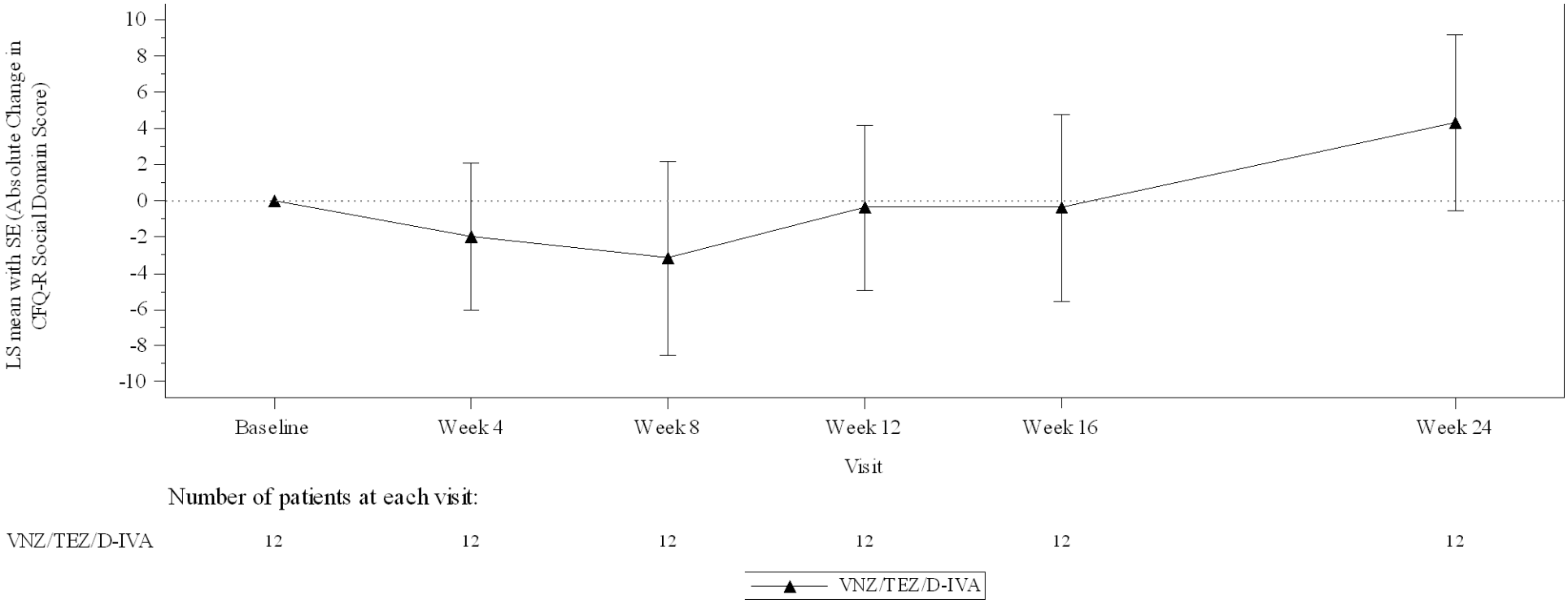
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Social
Region = Rest of World



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- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Social
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Social
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

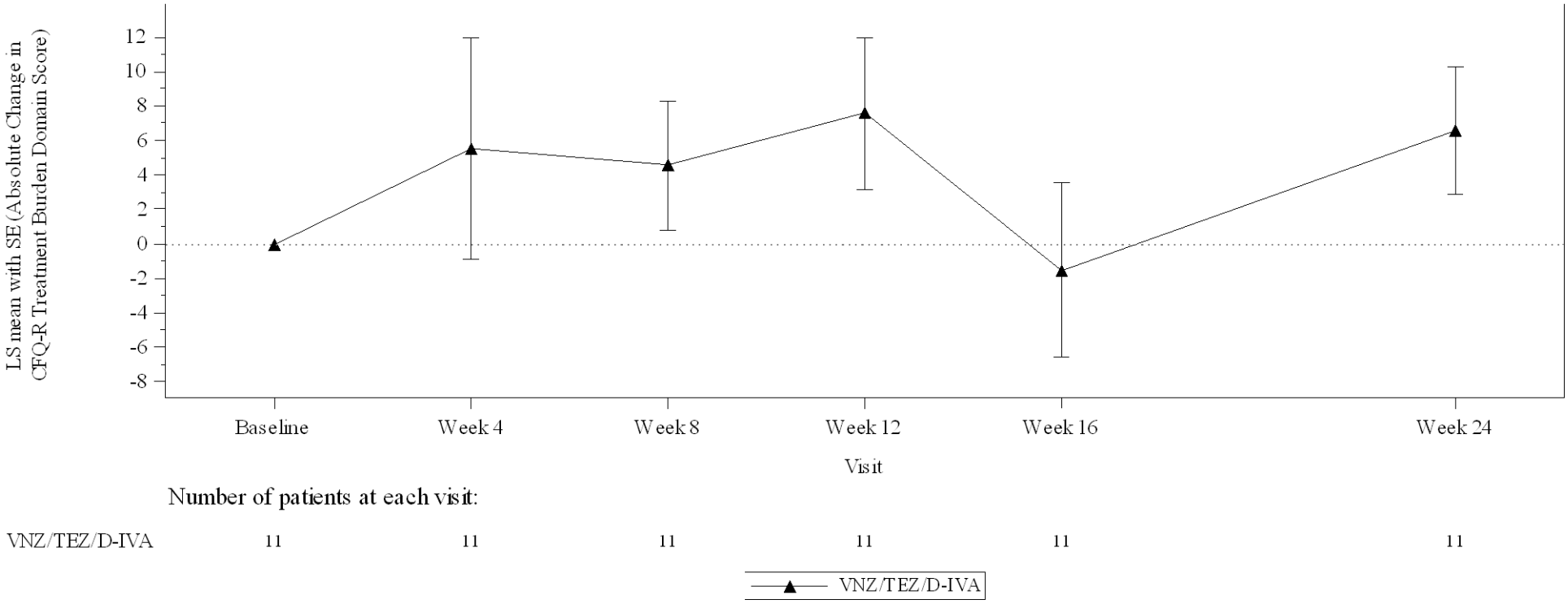
Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

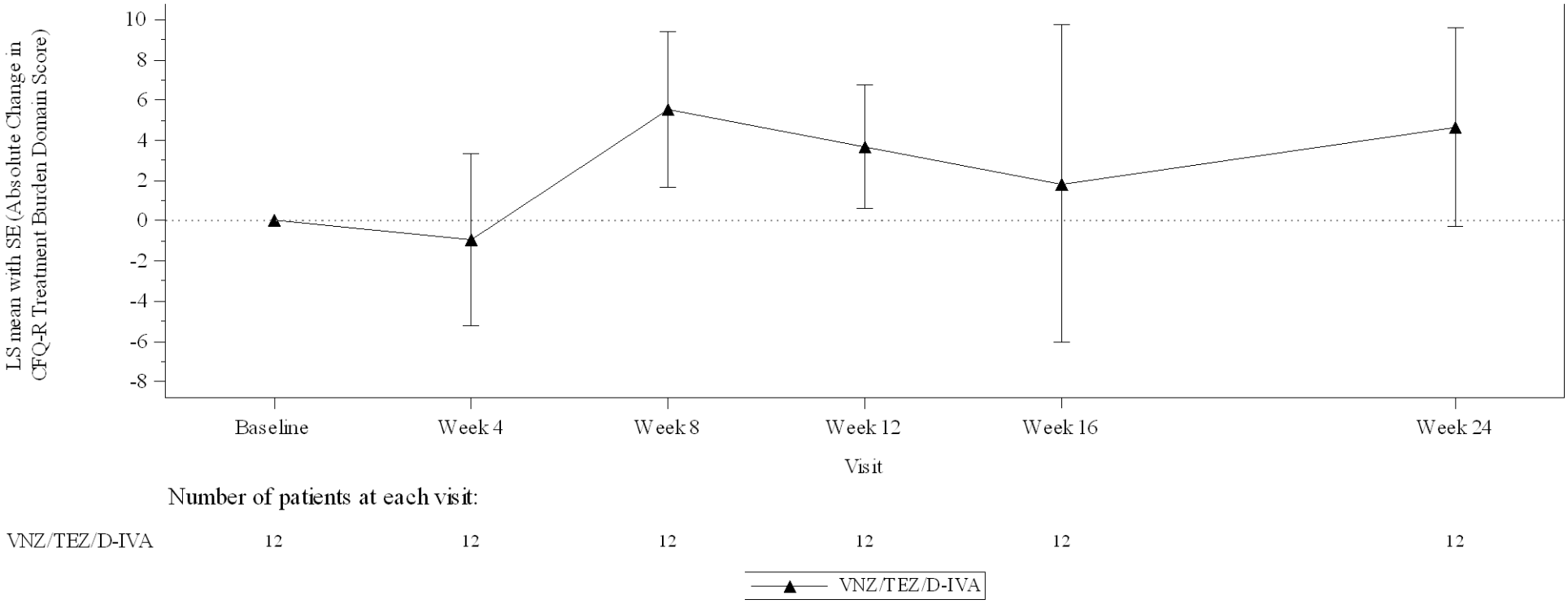
Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:15

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

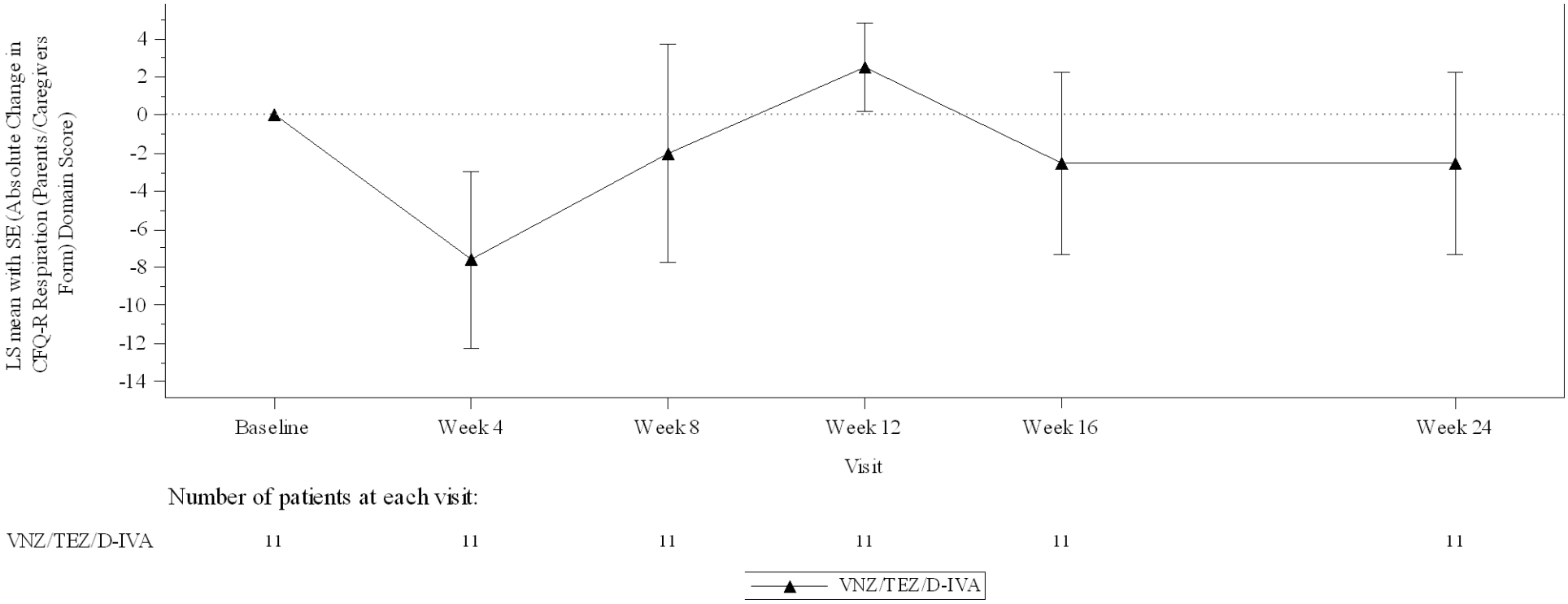
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

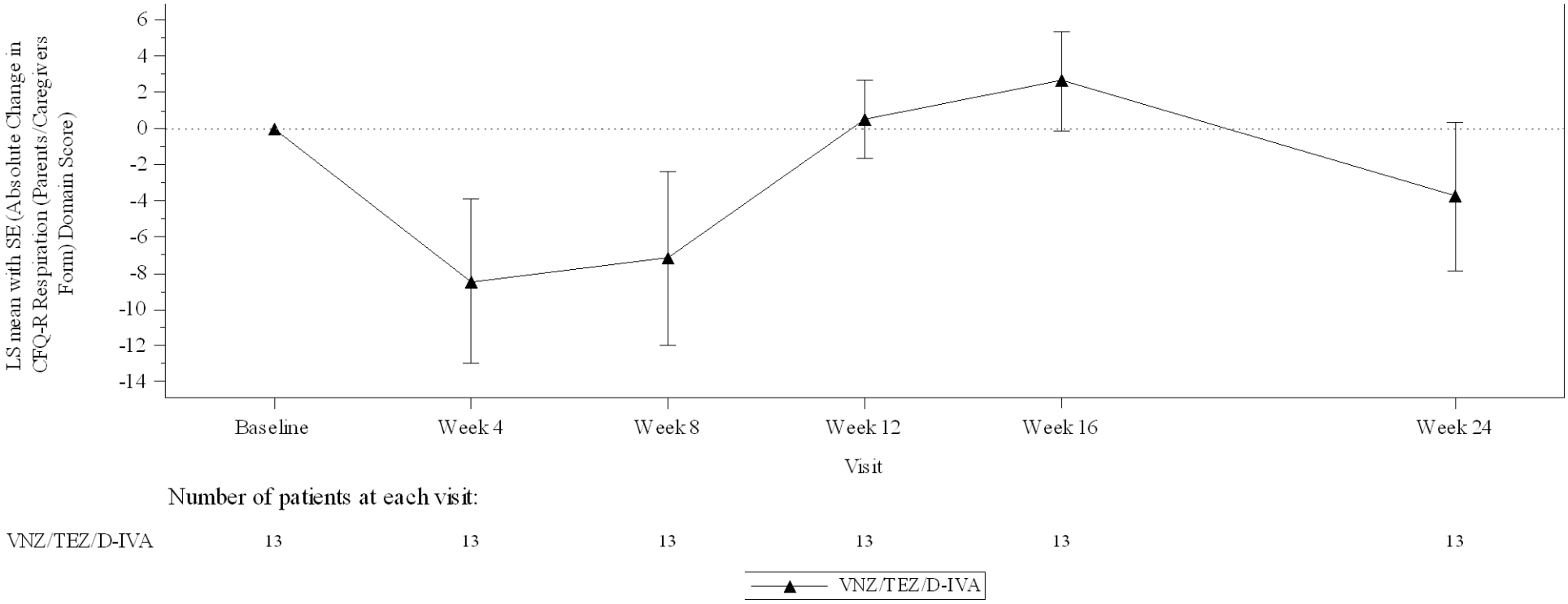
Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Region = Rest of World



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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

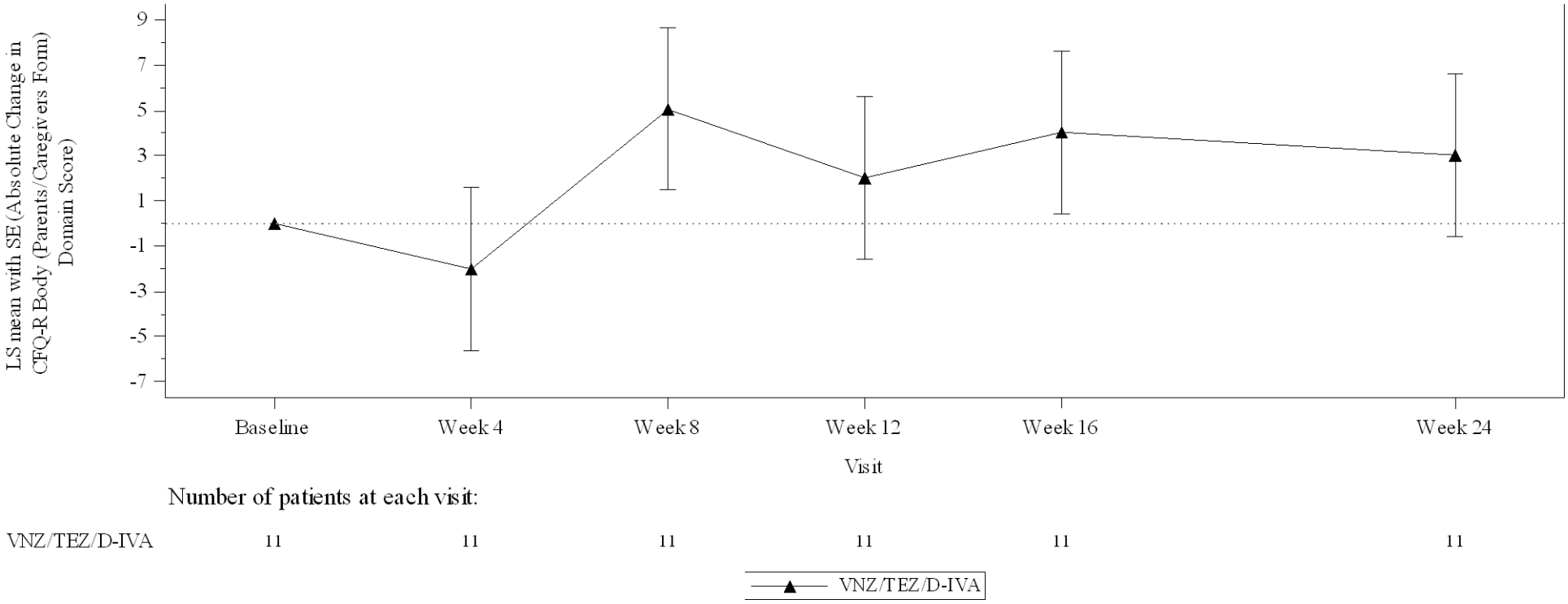
Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Region = North America



Number of patients at each visit:

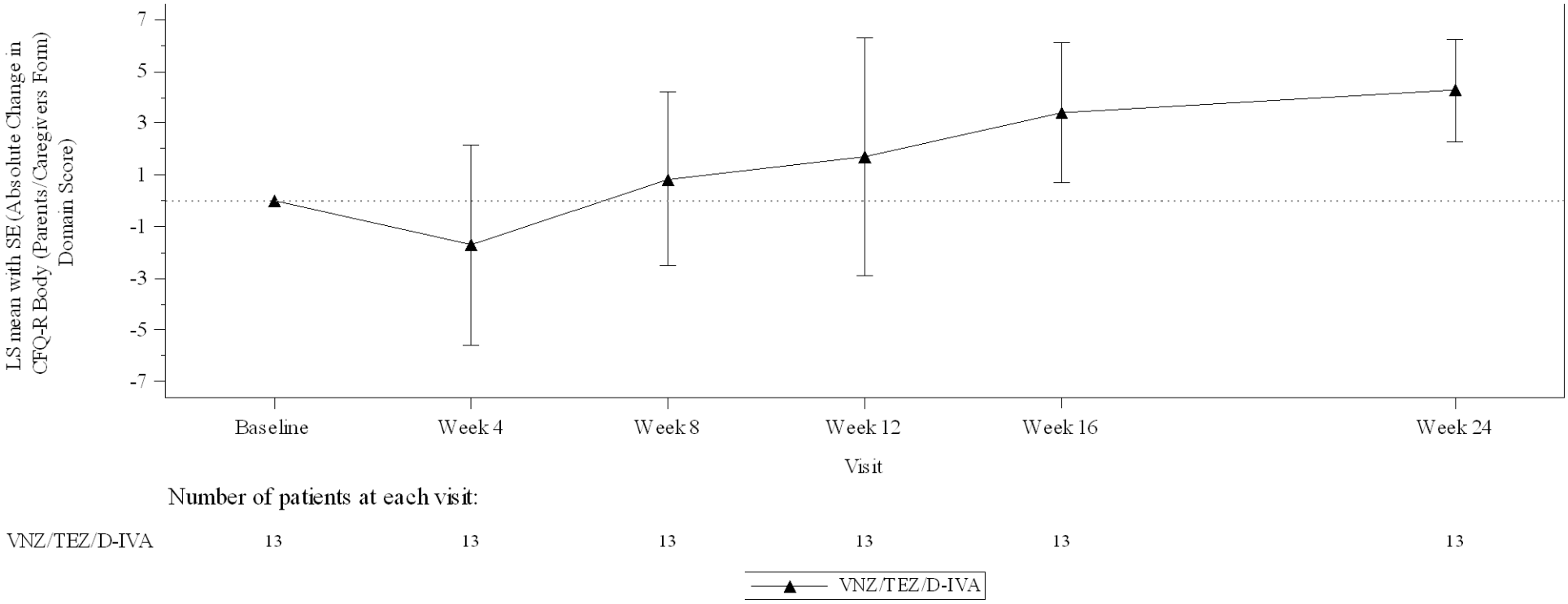
	Baseline	Week 4	Week 8	Week 12	Week 16	Week 24
VNZ/TEZ/D-IVA	11	11	11	11	11	11

VNZ/TEZ/D-IVA

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Region = Rest of World



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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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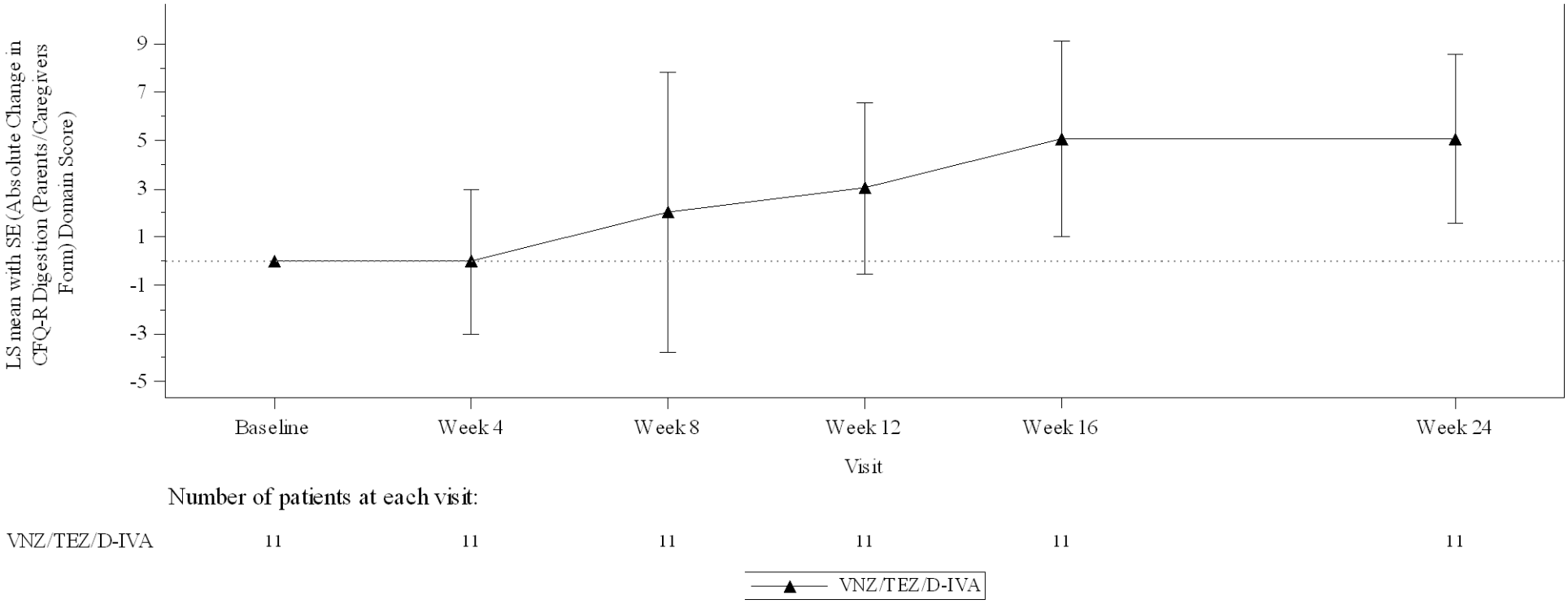
Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Region = North America



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- Baseline is defined as the pre-dose Day 1 value.
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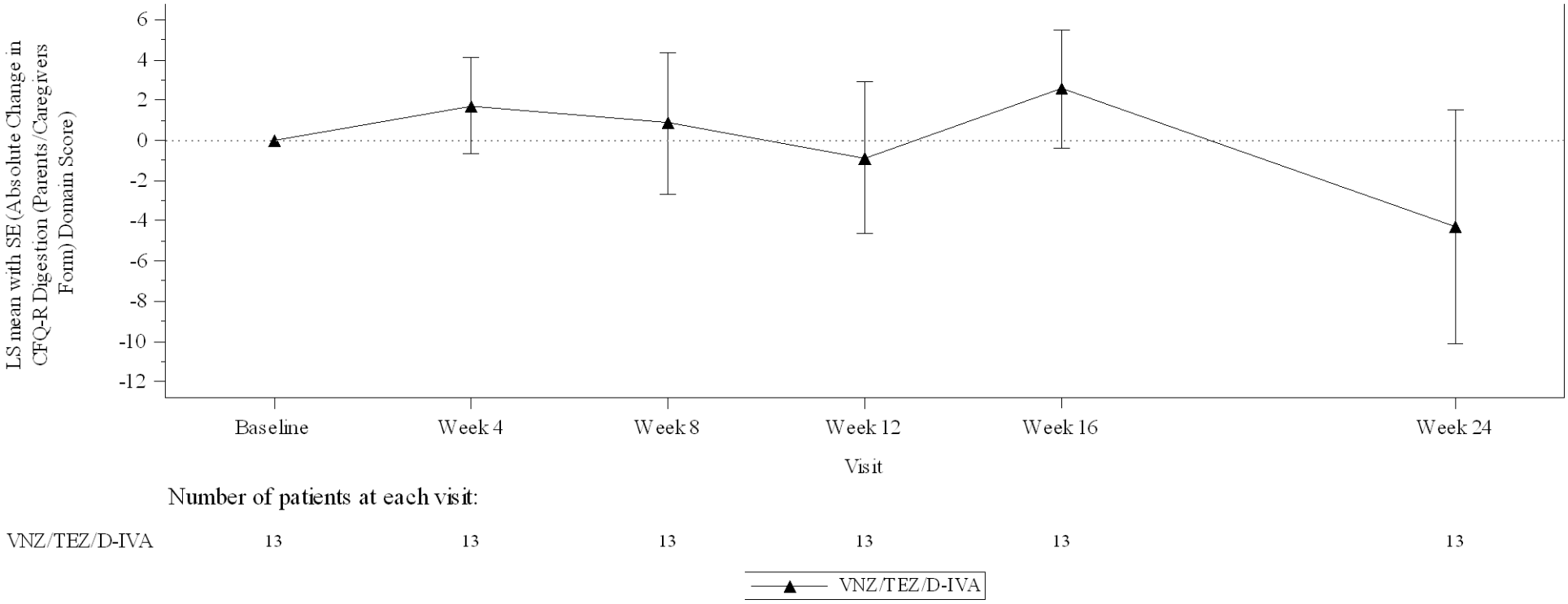
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World



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- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Region = North America

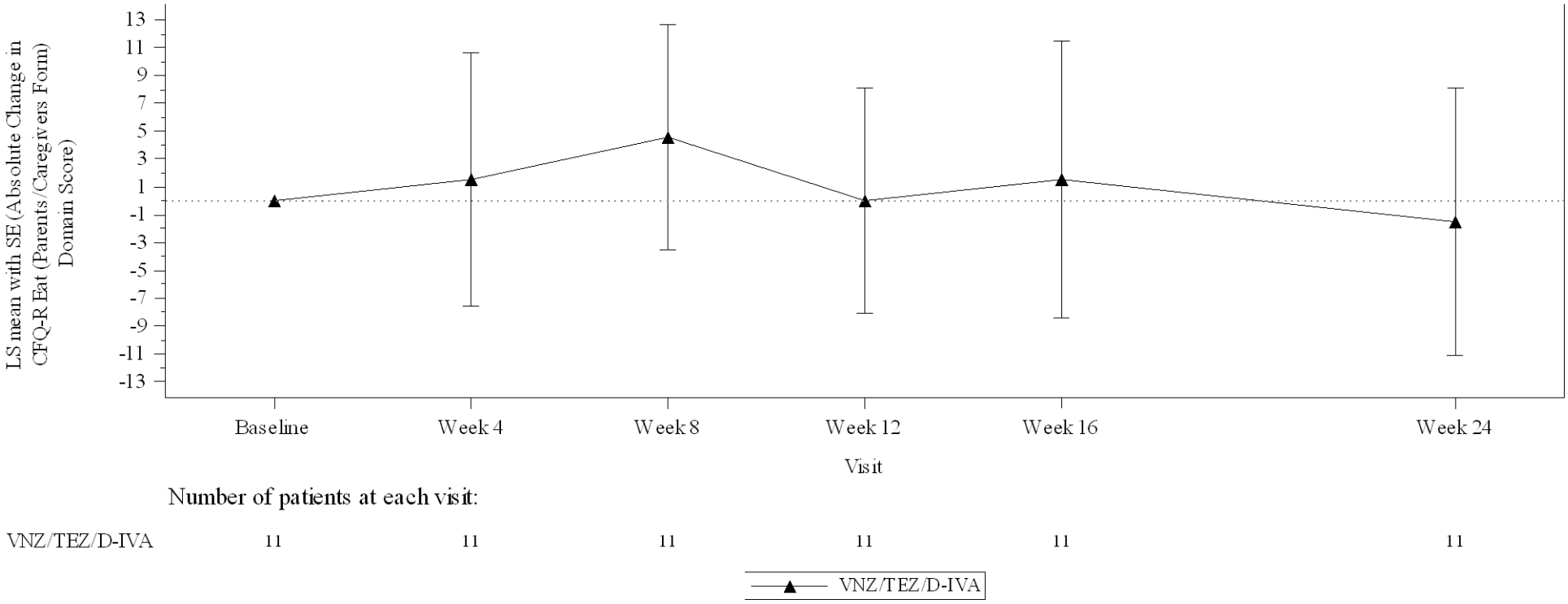

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

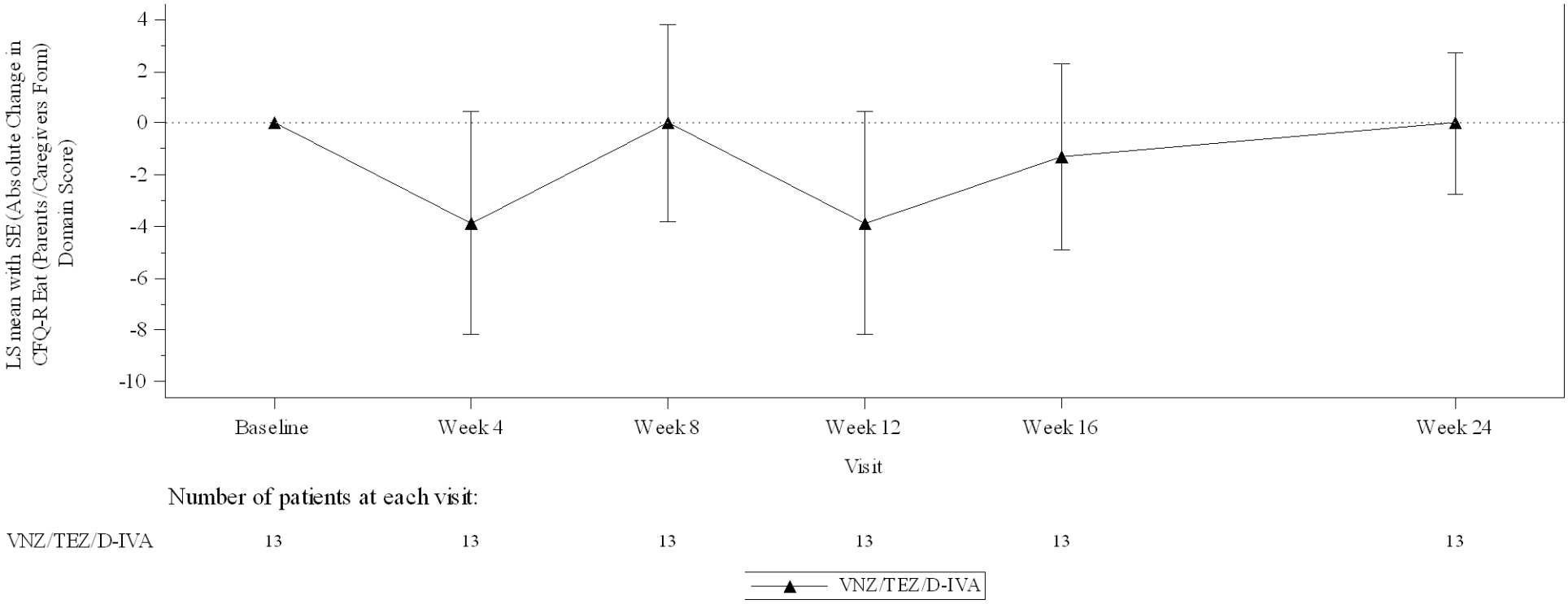

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Region = North America

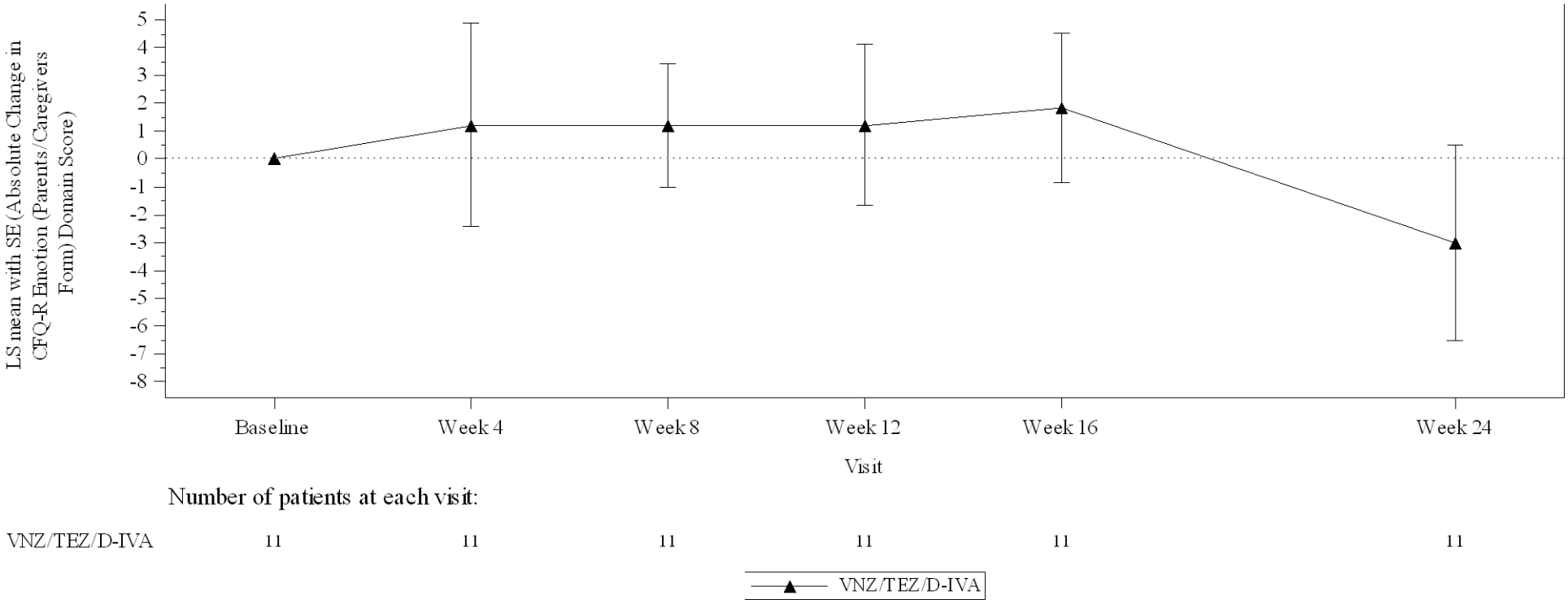

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

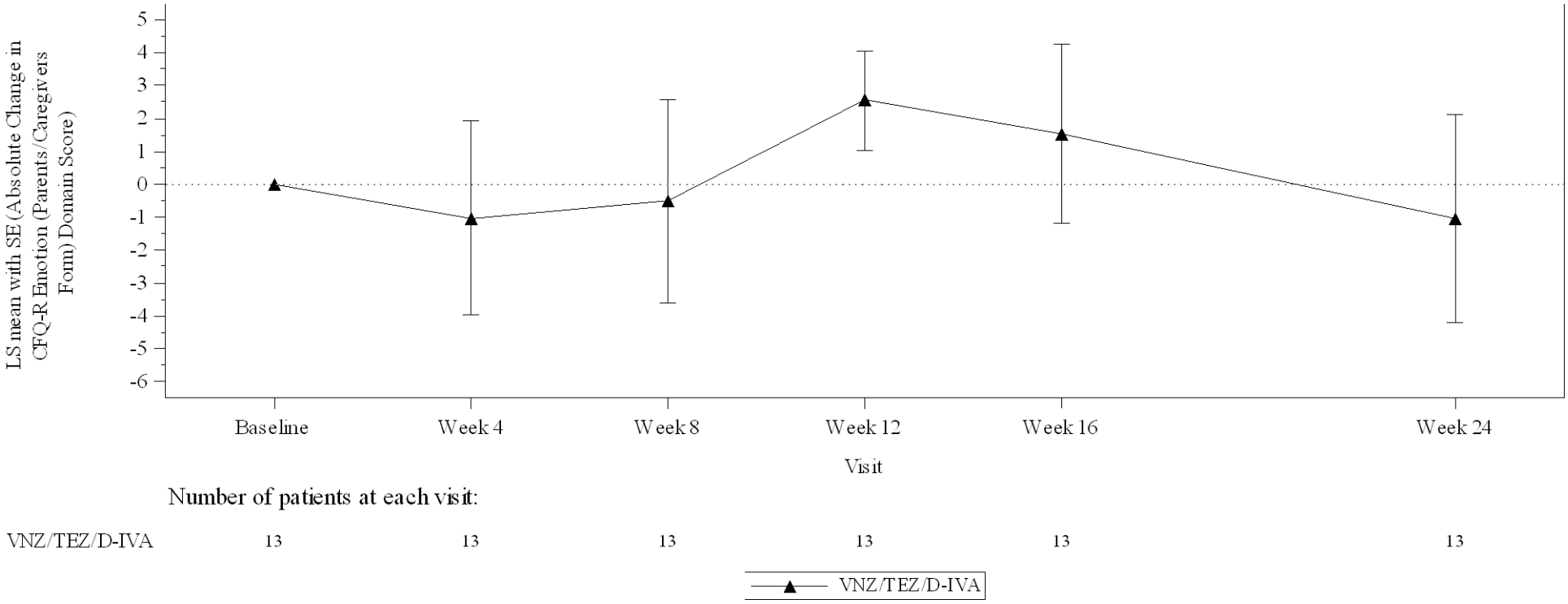

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

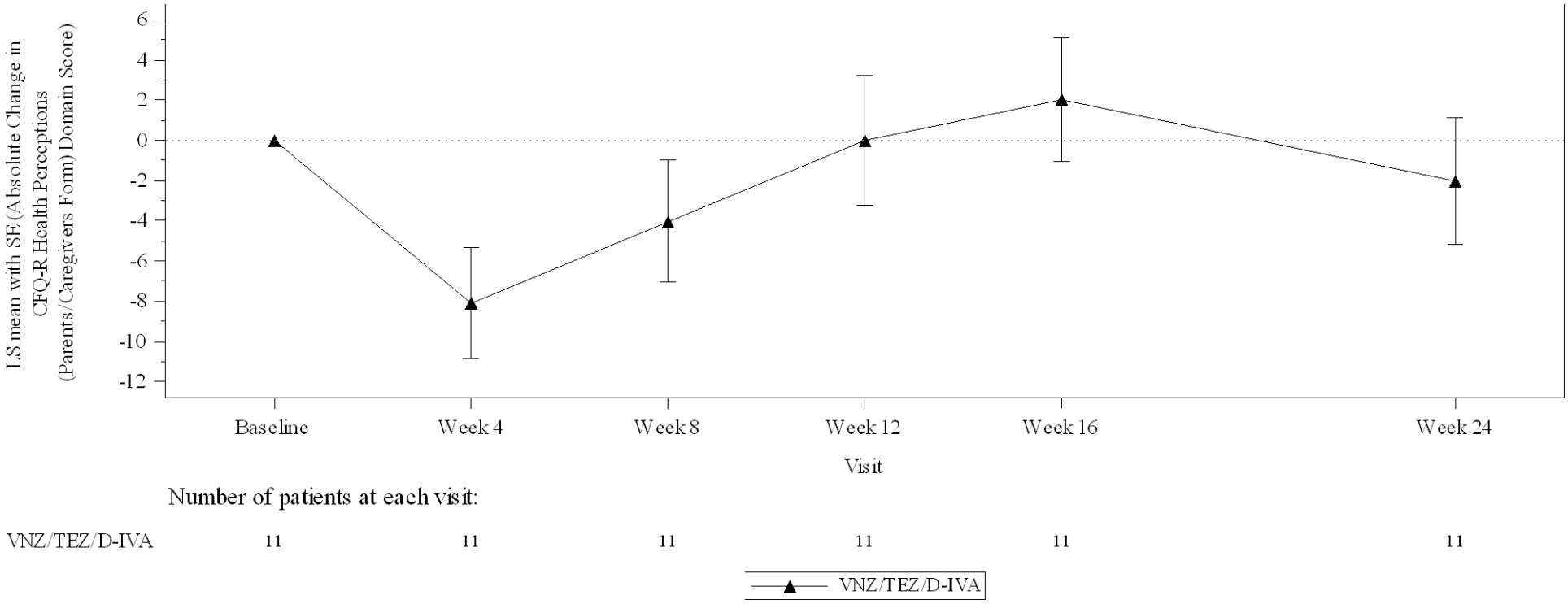

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

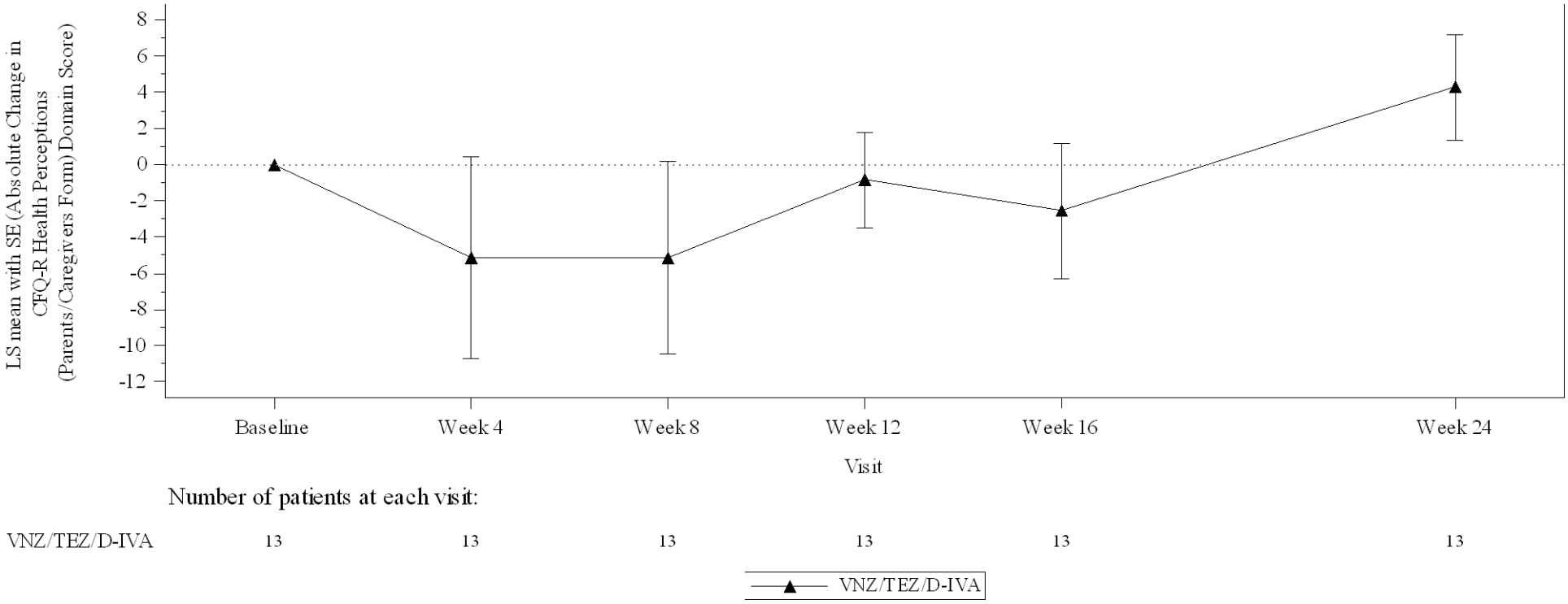

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Region = North America

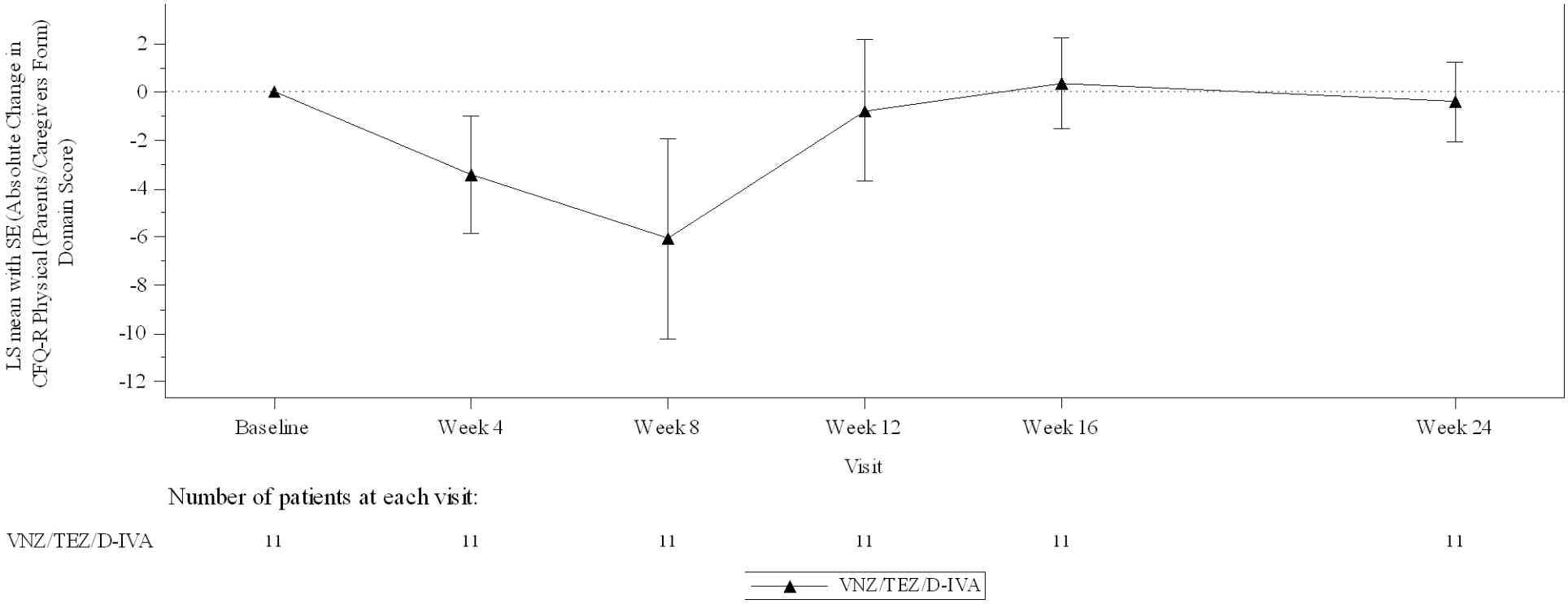

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

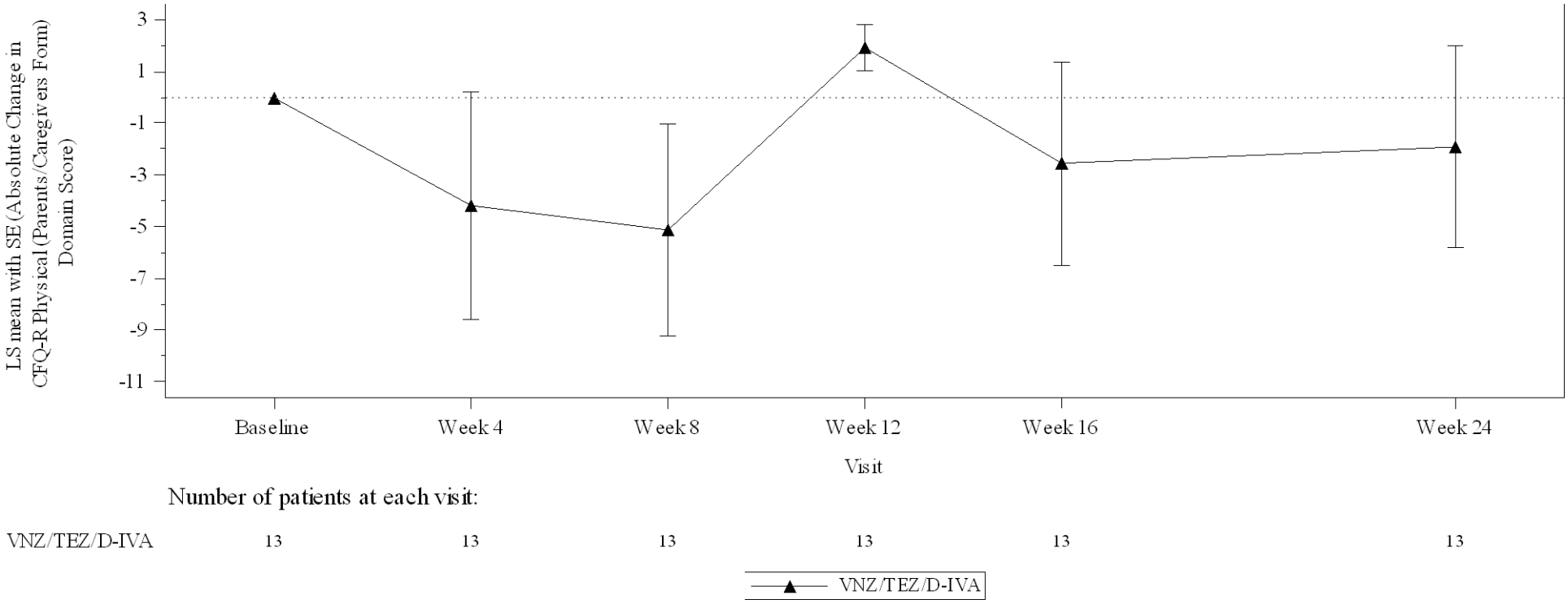

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Region = North America

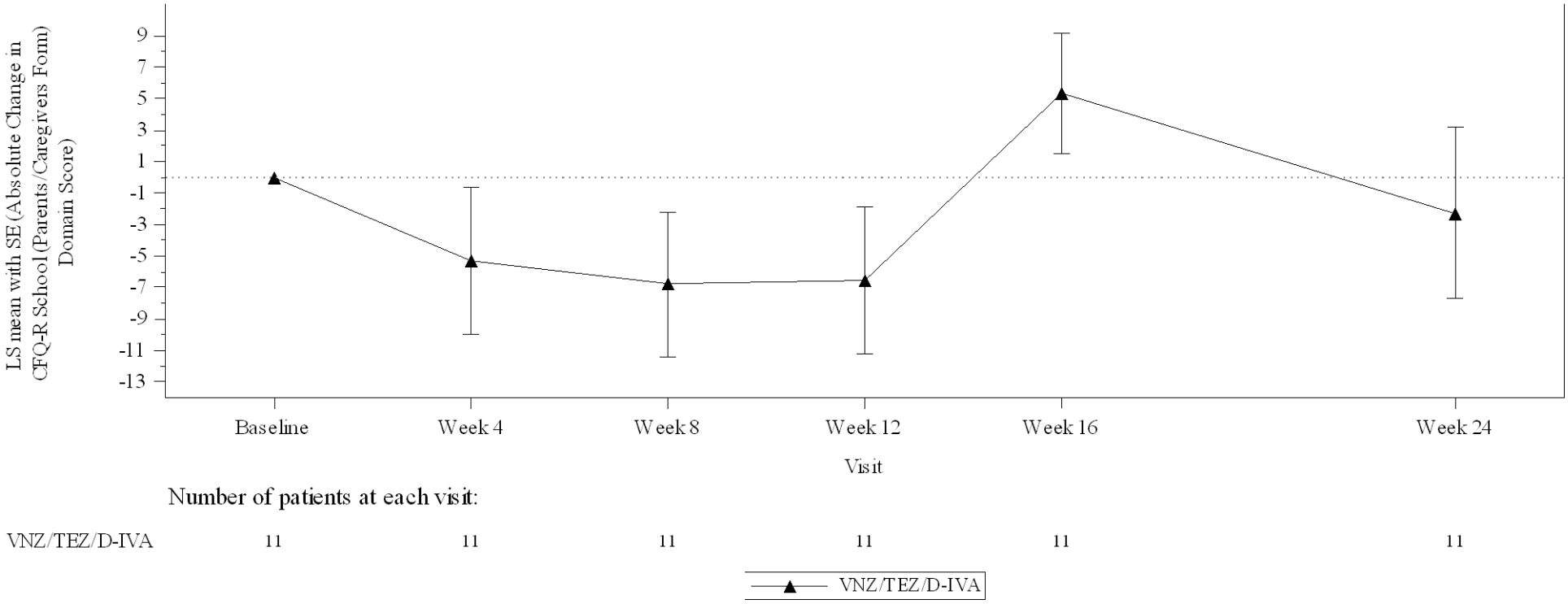

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Region = Rest of World

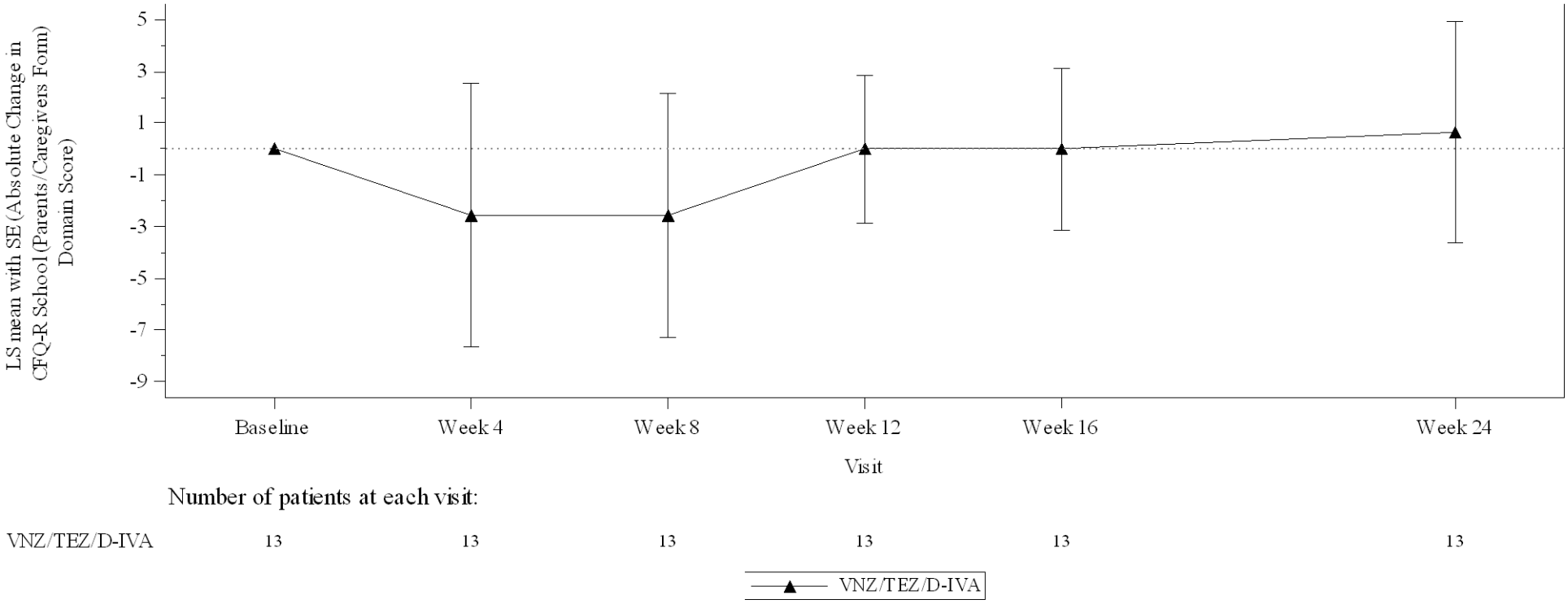

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

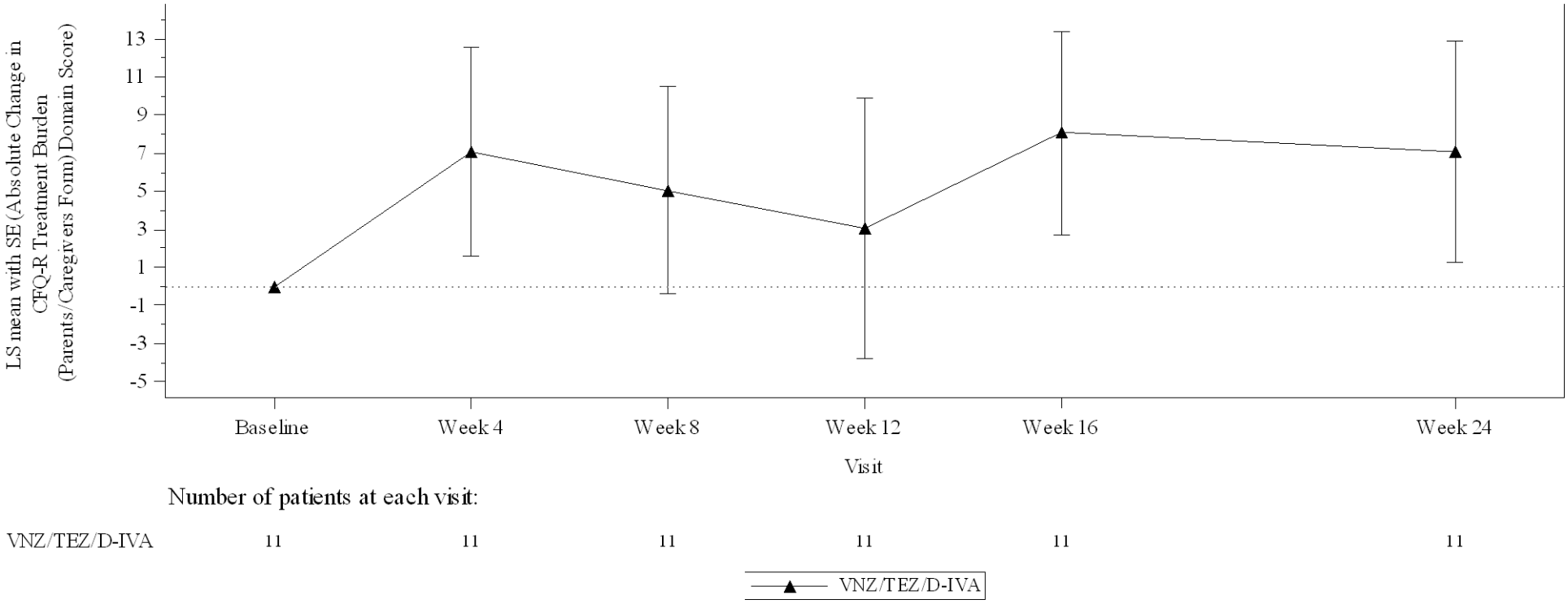

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

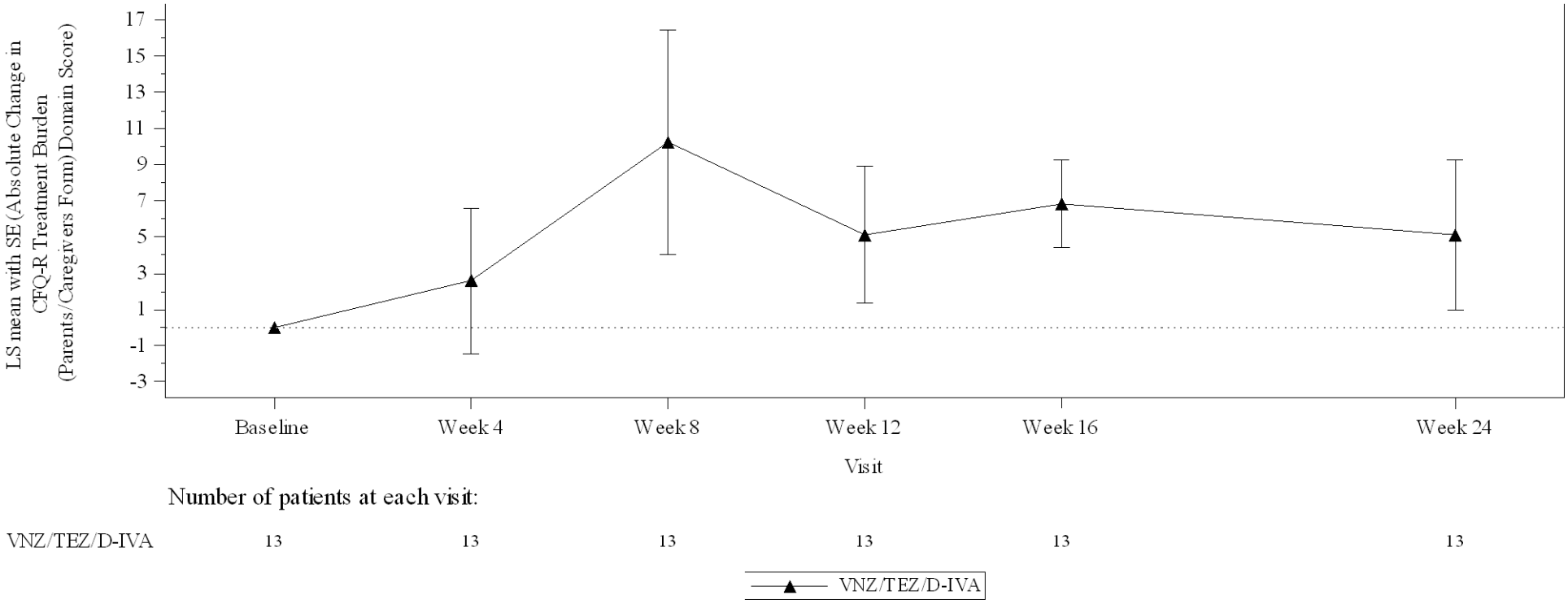

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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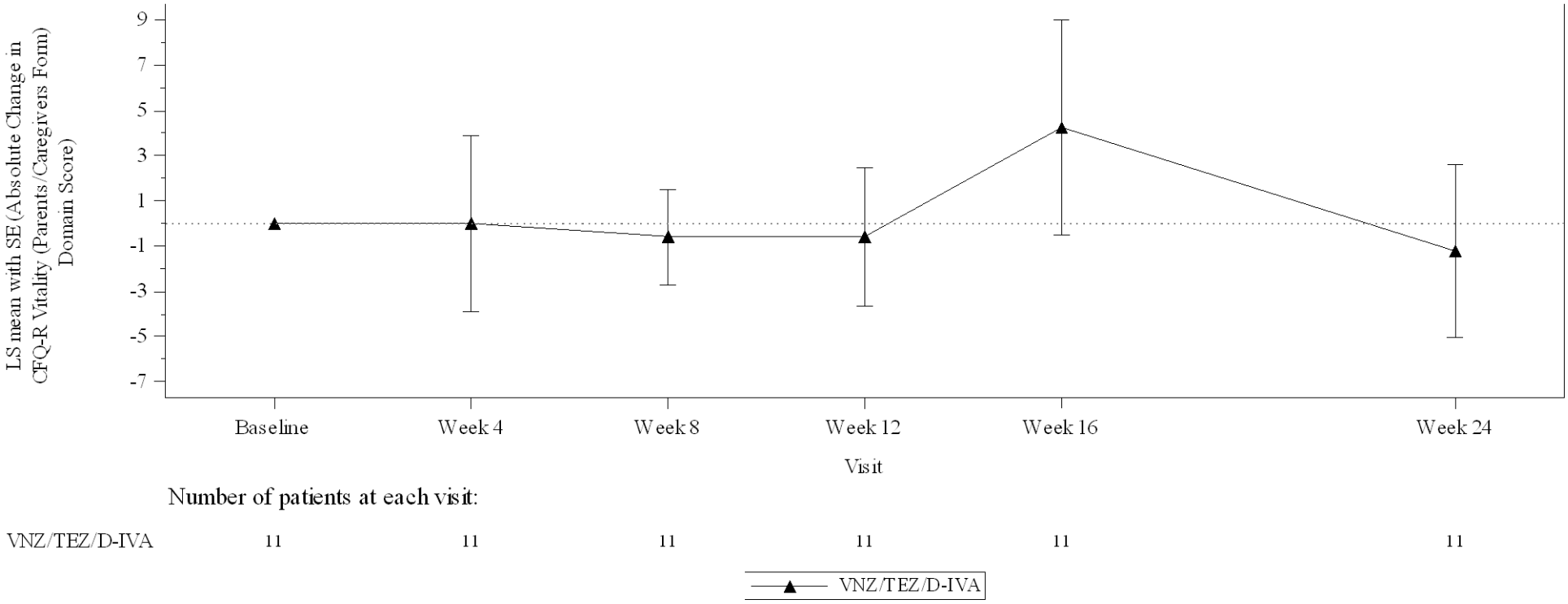
Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

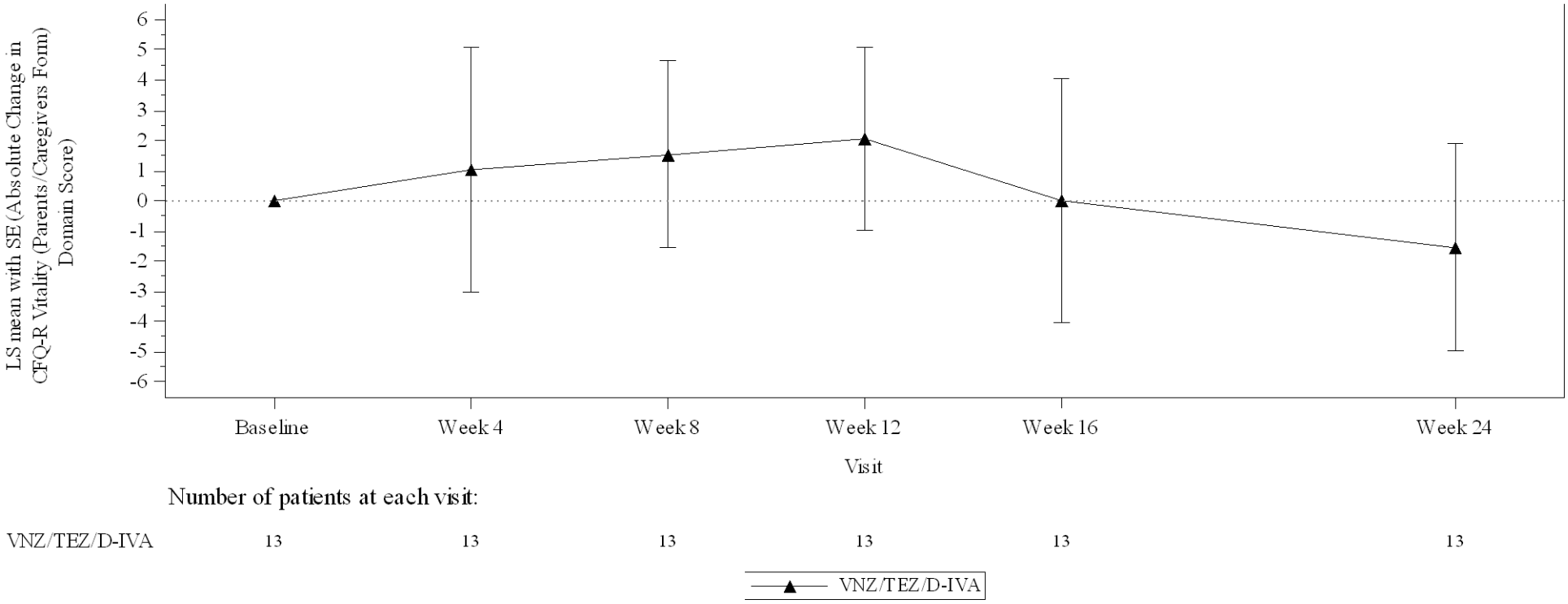
Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

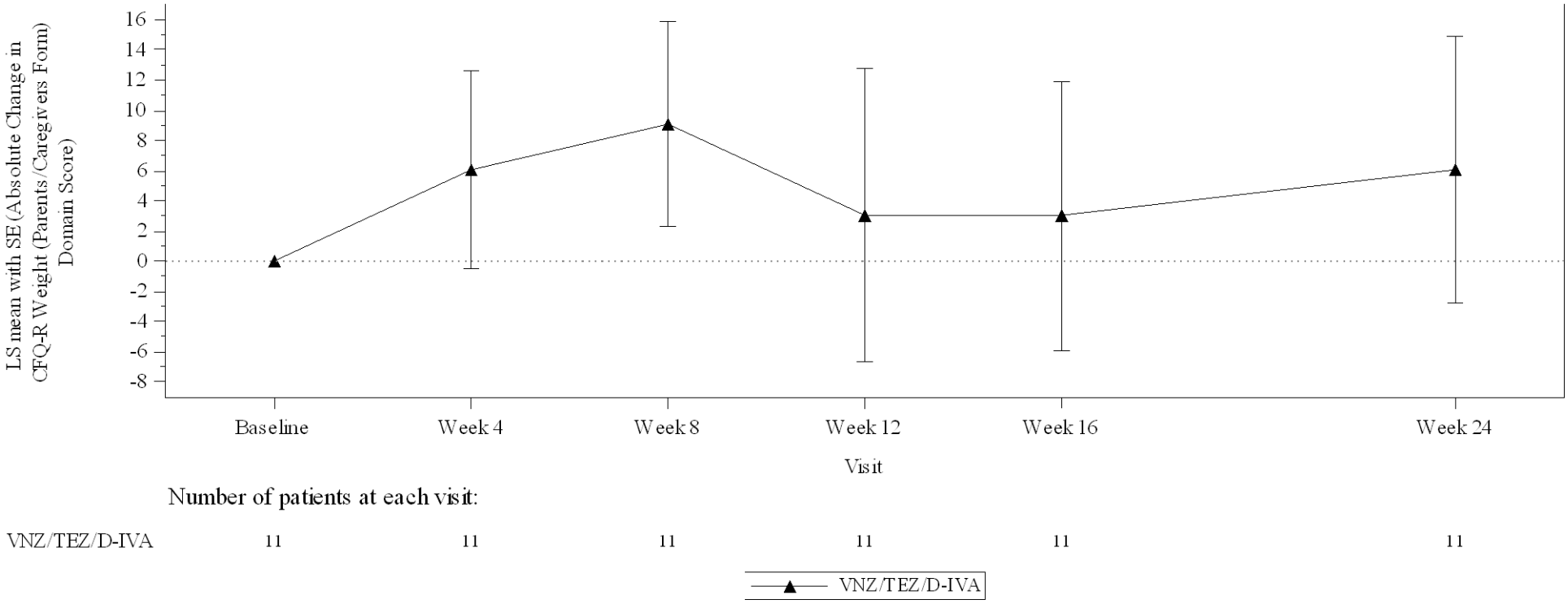
Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

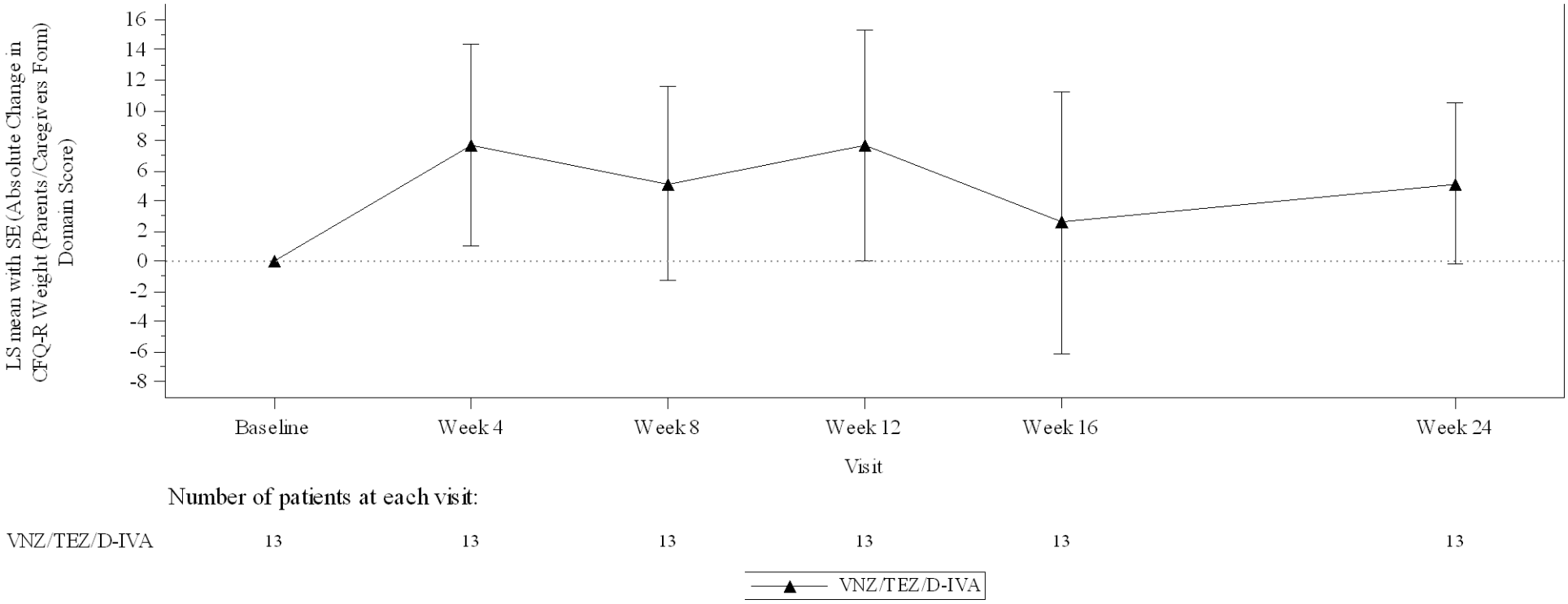
Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.14.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 1.2.2.14.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 1.2.2.14.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-km-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.14.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = Rest of the World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 1.2.2.14.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-km-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.14.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-km-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.15.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-hosp-km-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.15.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-hosp-km-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.15.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-hosp-km-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.15.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = Rest of the World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-hosp-km-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.15.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 1.2.2.15.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-hosp-km-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.16.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-iv-km-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.16.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-iv-km-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.16.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-iv-km-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.16.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = Rest of the World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-iv-km-24wks-sub-b1-fmf.sas Creation: 06FEB2025 10:16

Figure 1.2.2.16.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

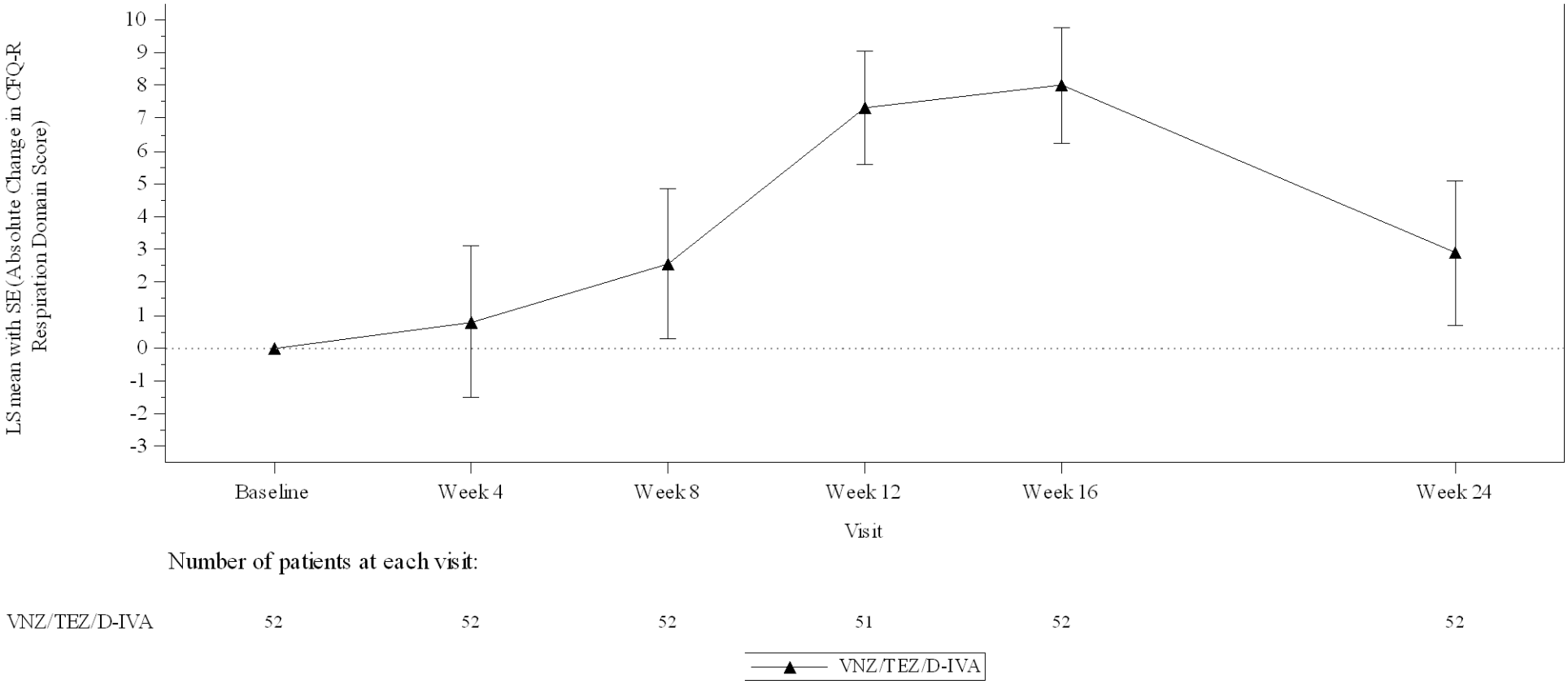
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 1.2.2.16.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

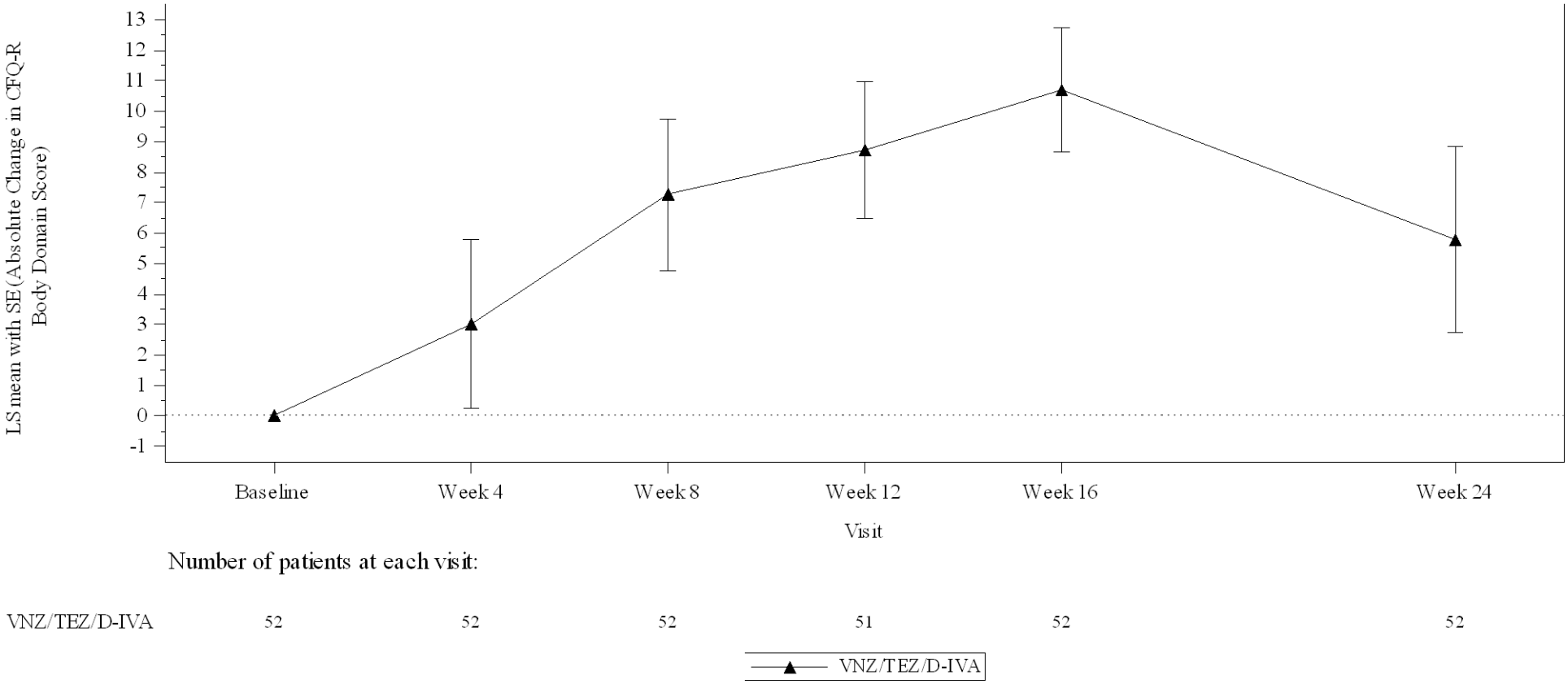
Figure 2.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Respiration



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1-nonfmf.sas Creation: 06FEB2025 10:17

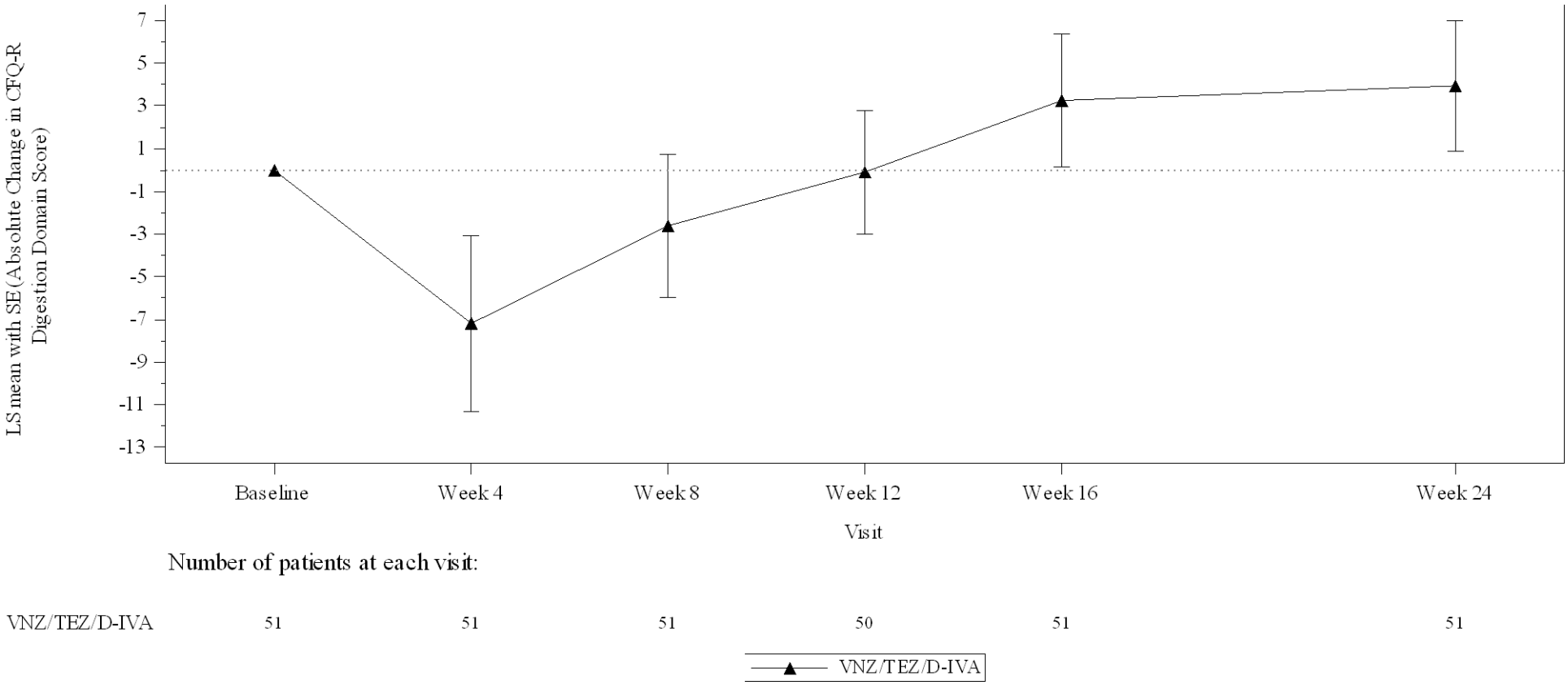
Figure 2.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Body



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

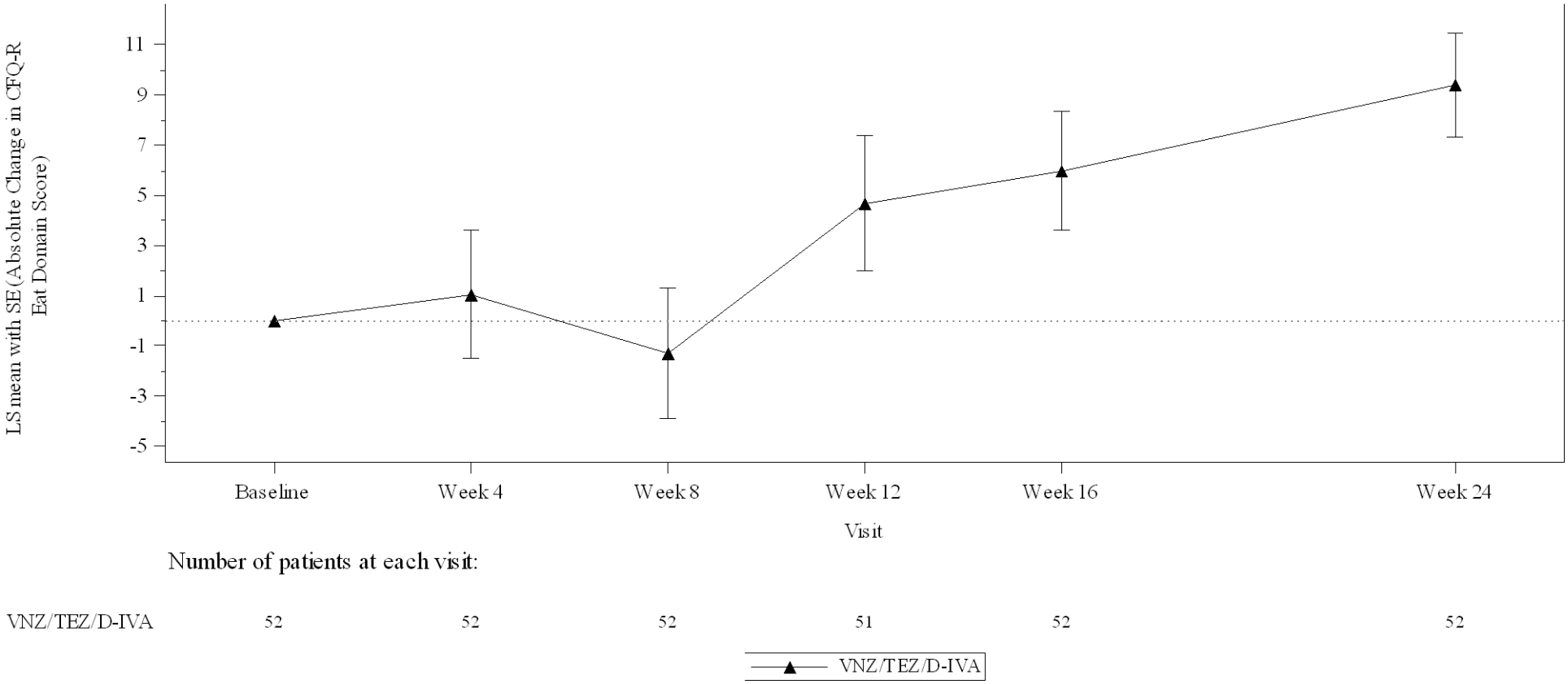
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1-nonfmf.sas Creation: 06FEB2025 10:17

Figure 2.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Digestion



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Eat



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

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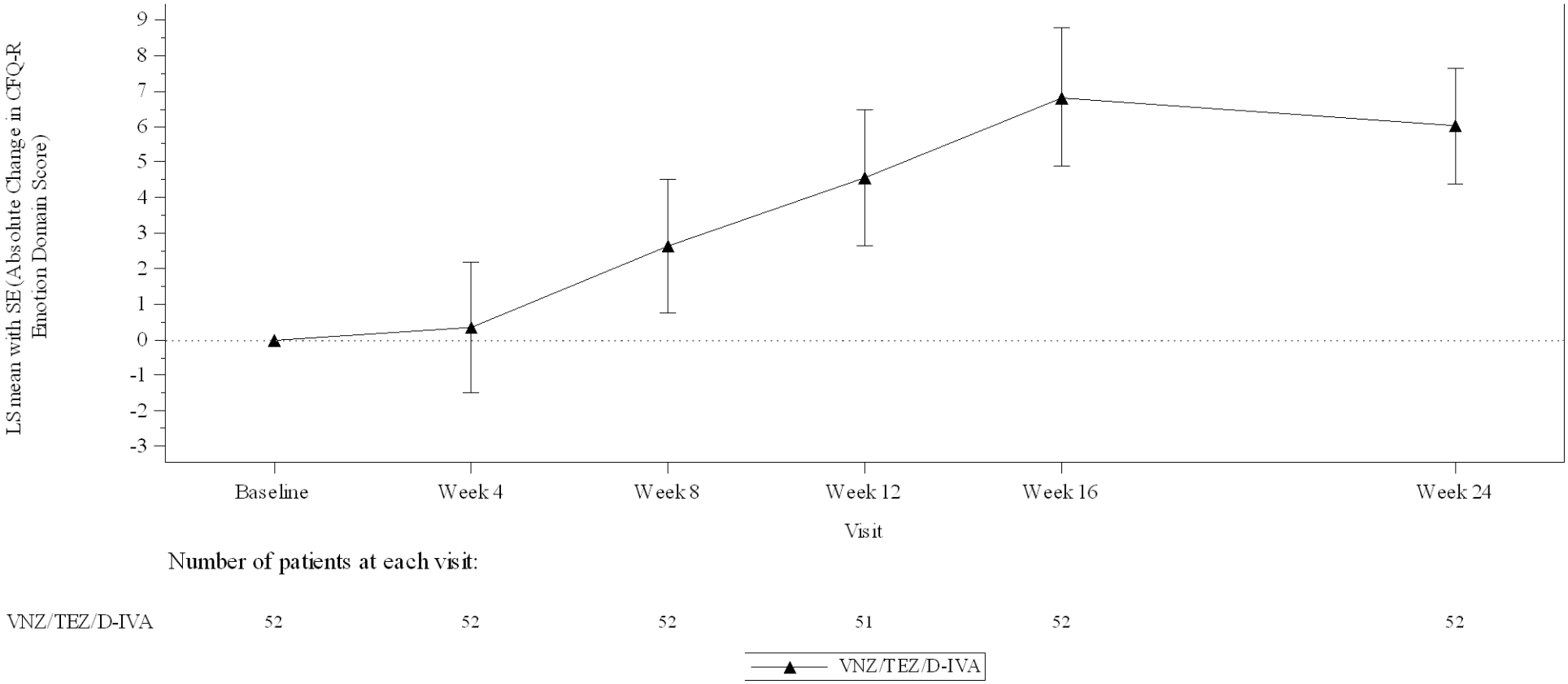
Figure 2.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Emotion



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

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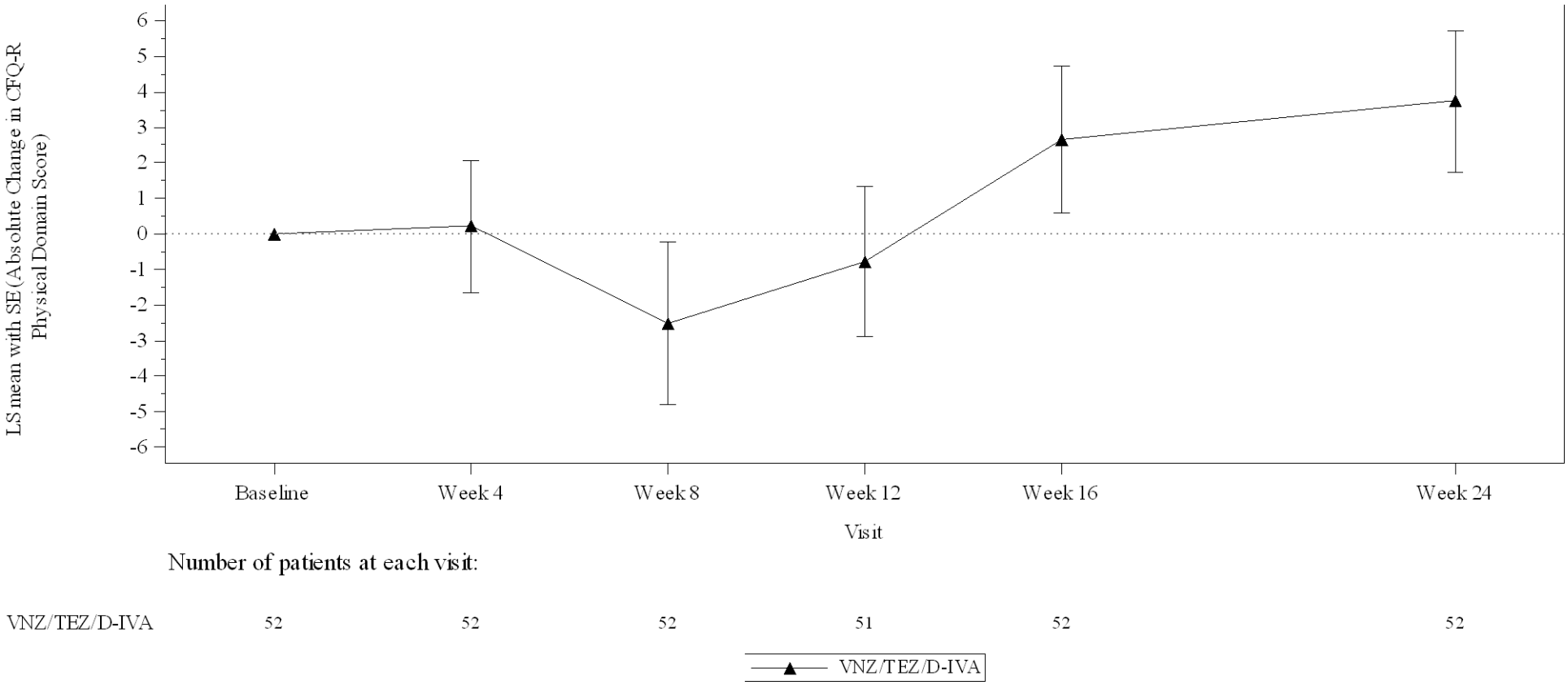
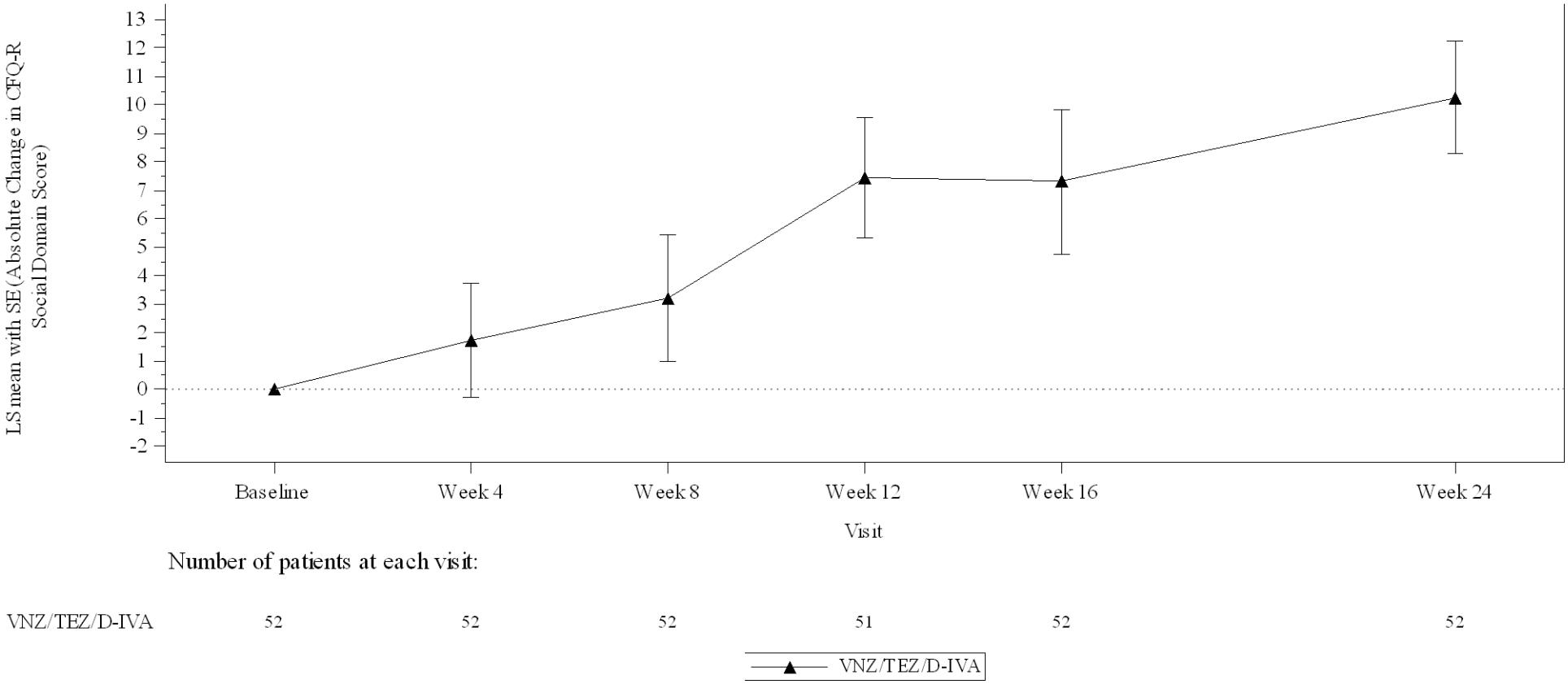
Figure 2.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Physical



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1-nonfmf.sas Creation: 06FEB2025 10:17

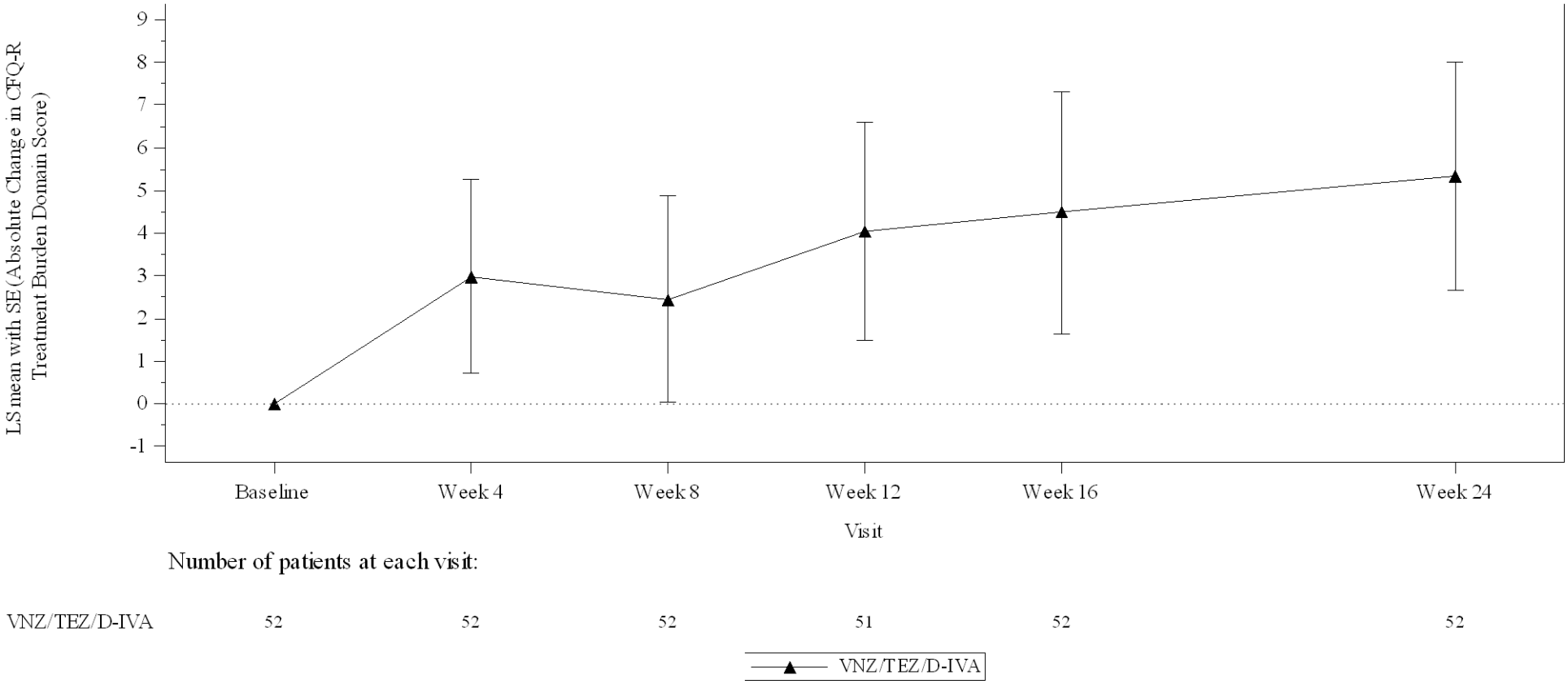
Figure 2.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Social



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1-nonfmf.sas Creation: 06FEB2025 10:17

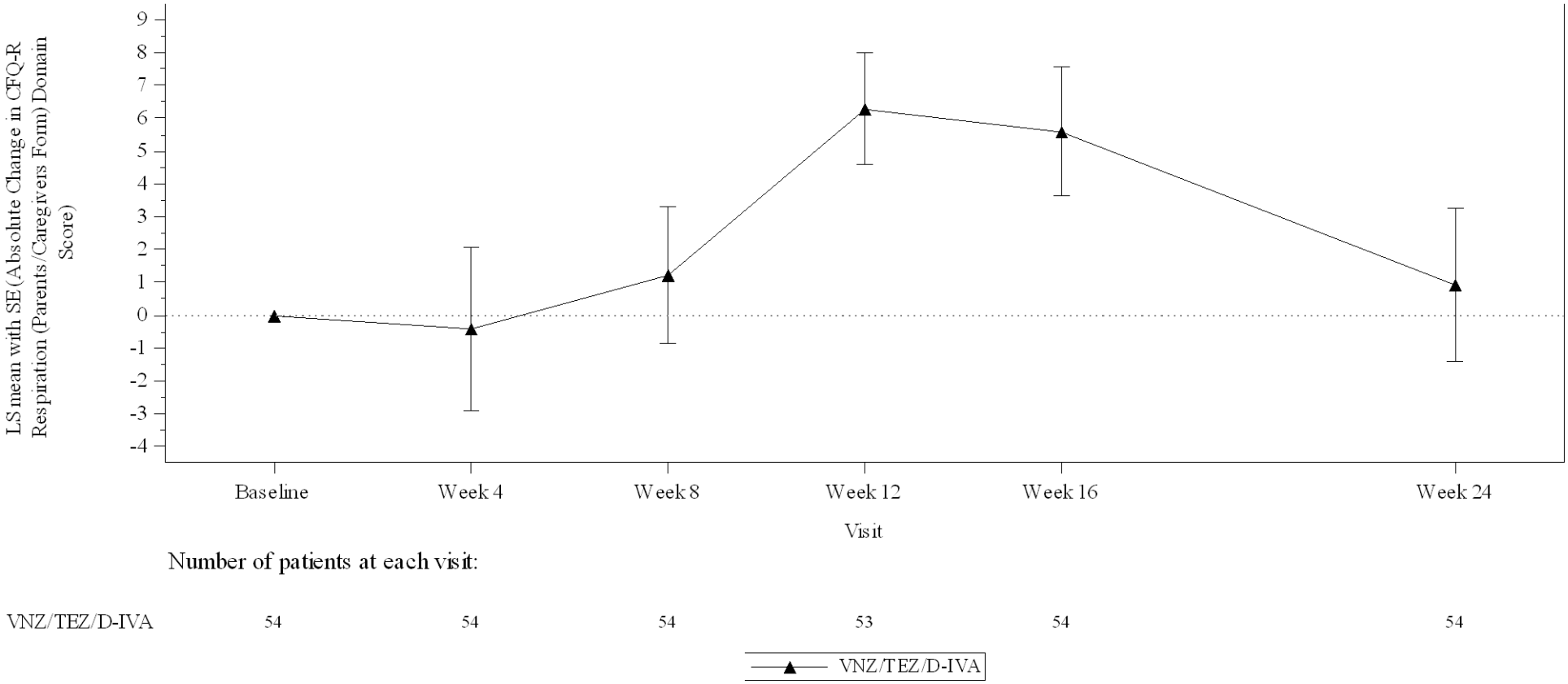
Figure 2.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Treatment Burden



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

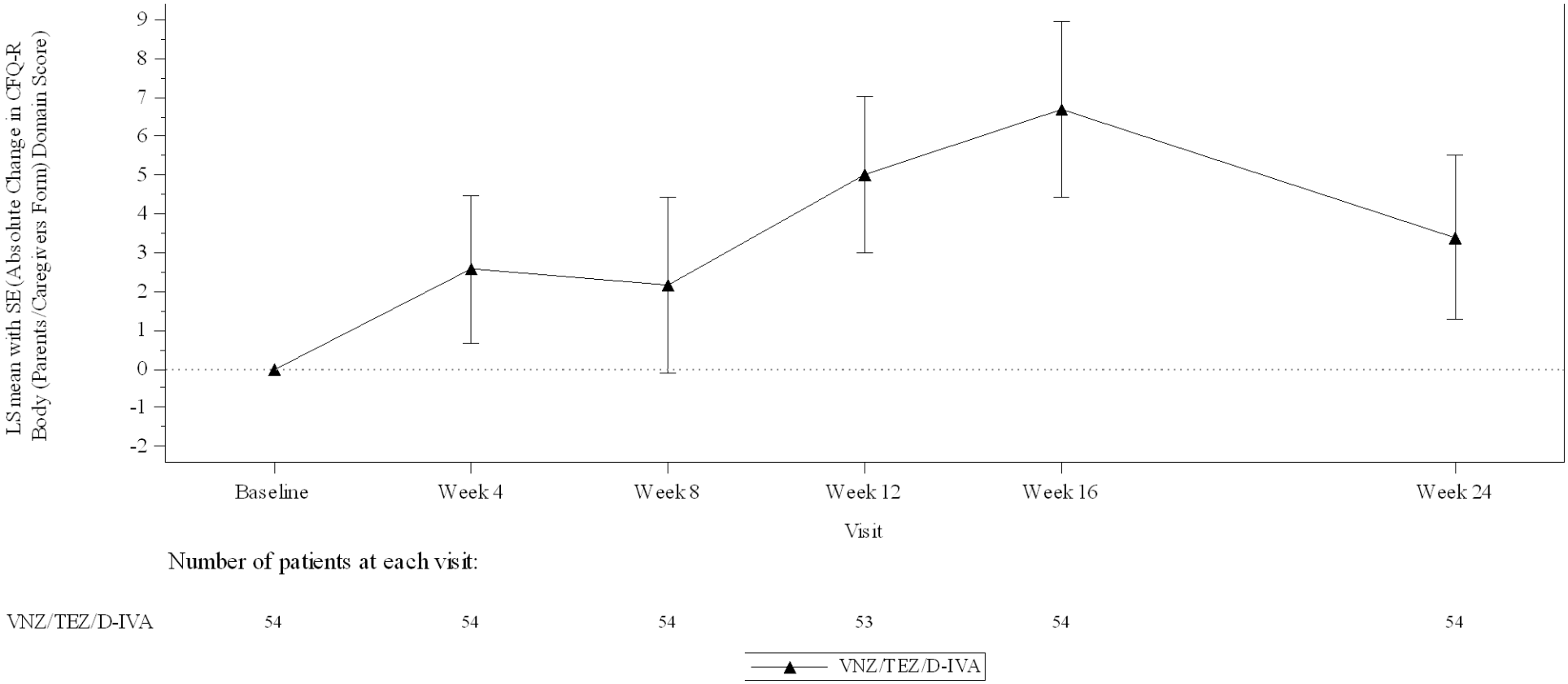
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1-nonfmf.sas Creation: 06FEB2025 10:17

Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Body (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

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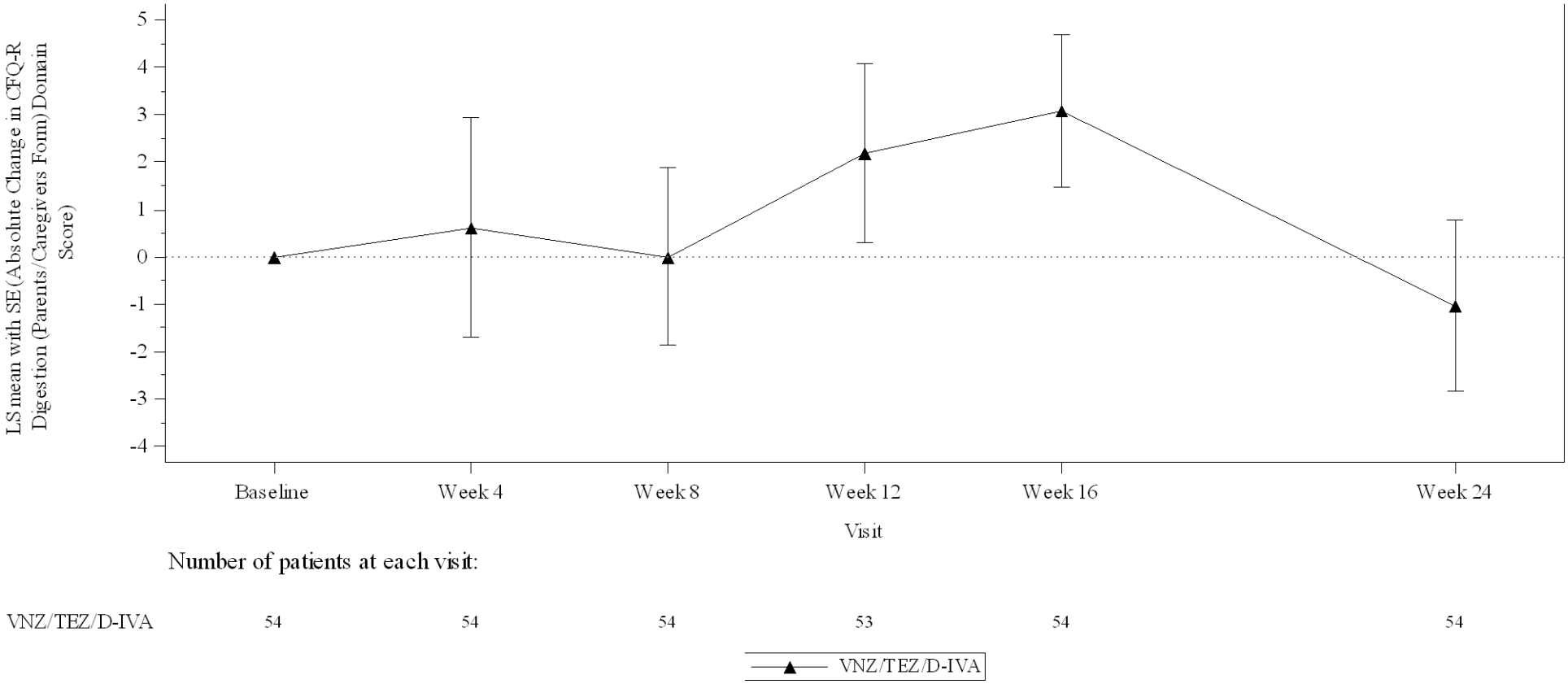
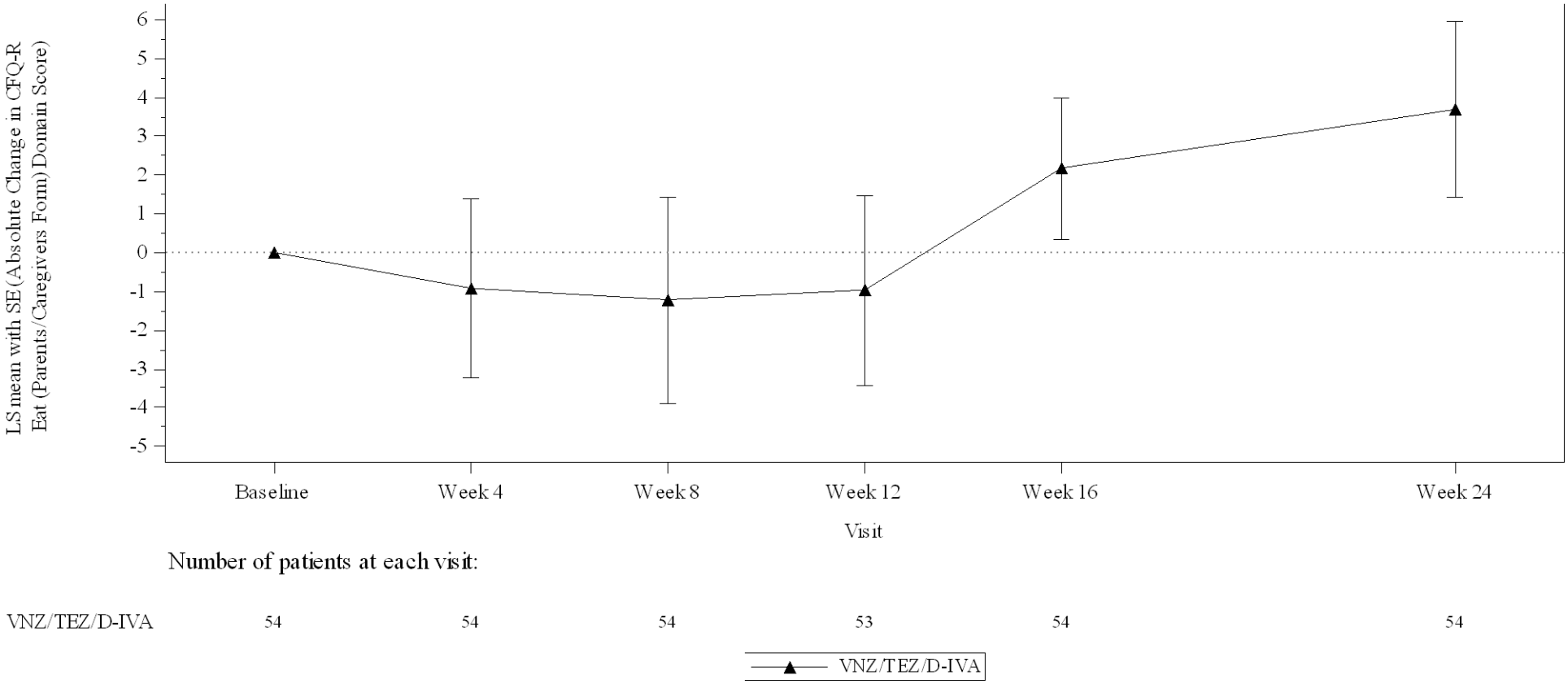
Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-nonfmf.sas Creation: 06FEB2025 10:17

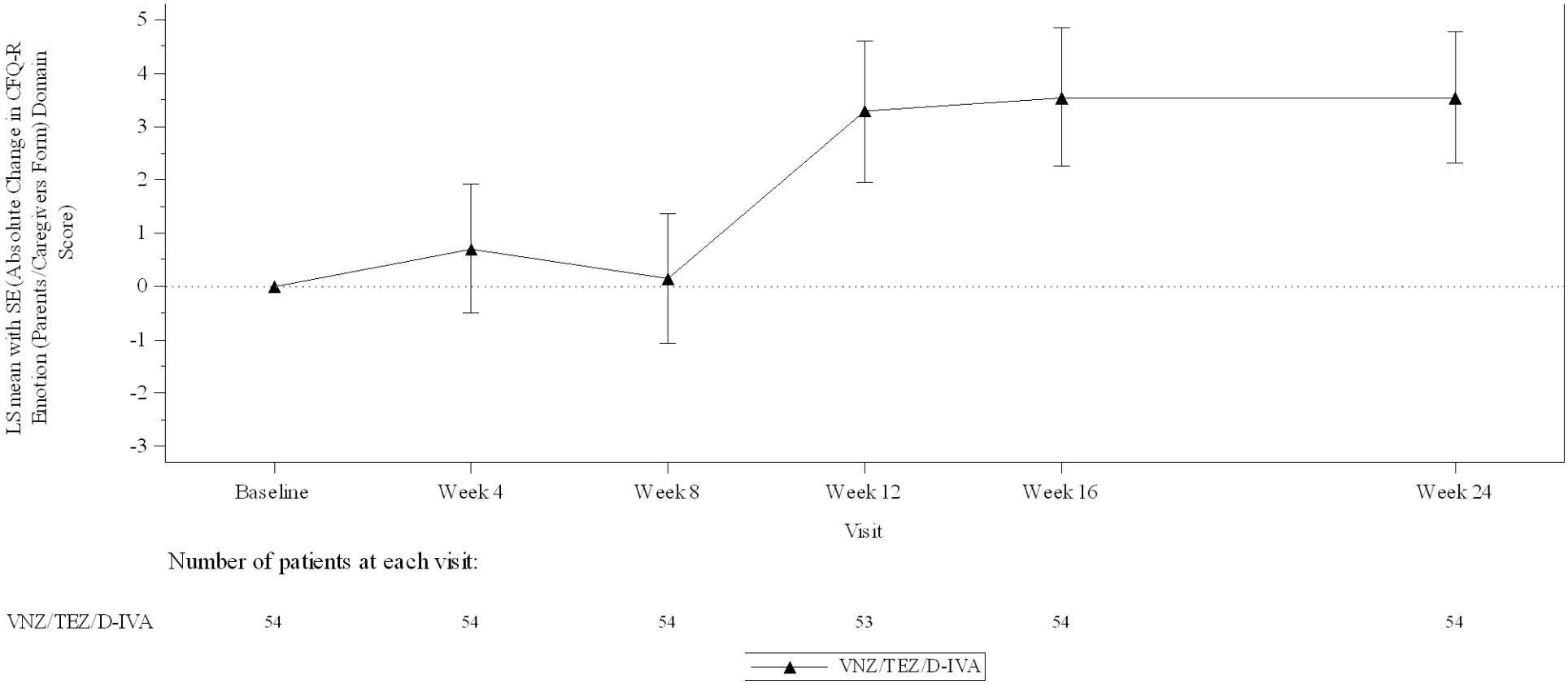
Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-nonfmf.sas Creation: 06FEB2025 10:17

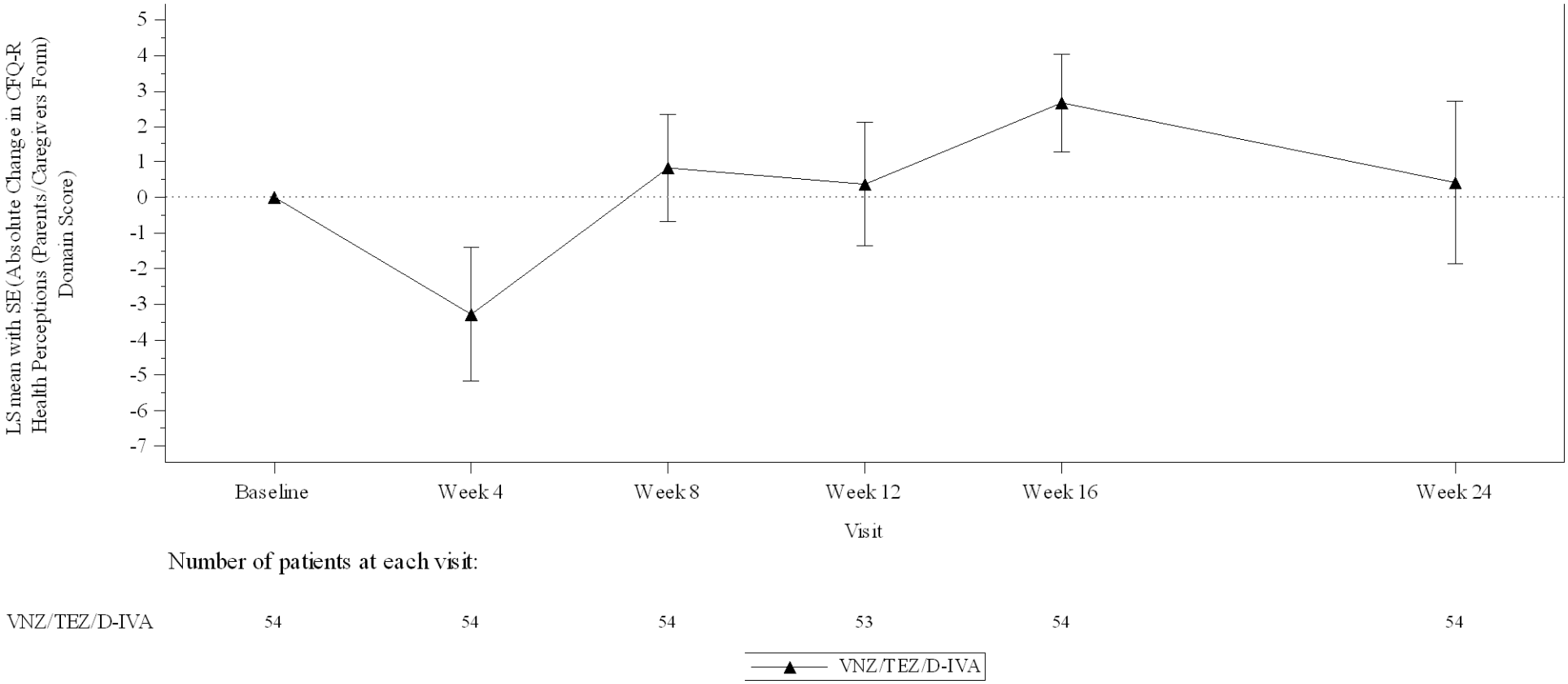
Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-nonfmf.sas Creation: 06FEB2025 10:17

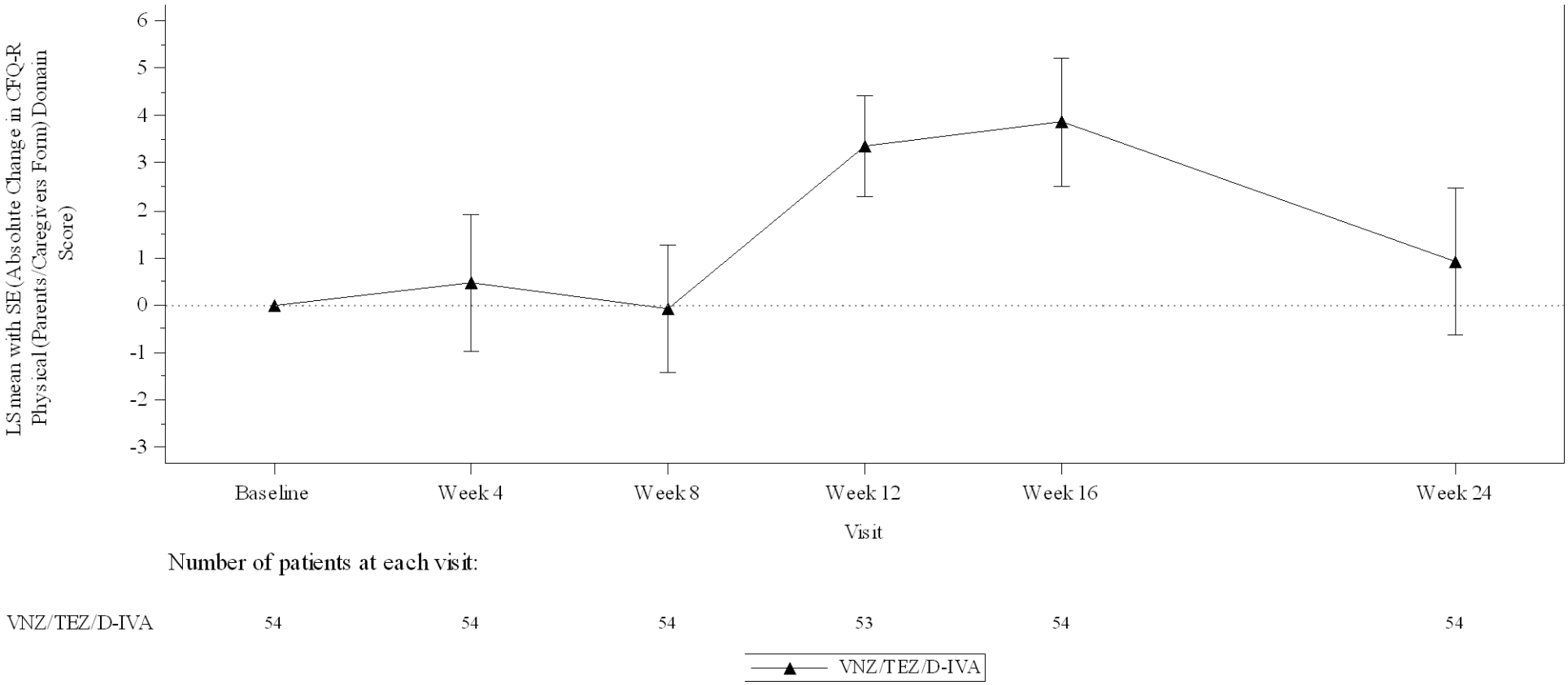
Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-nonfmf.sas Creation: 06FEB2025 10:17

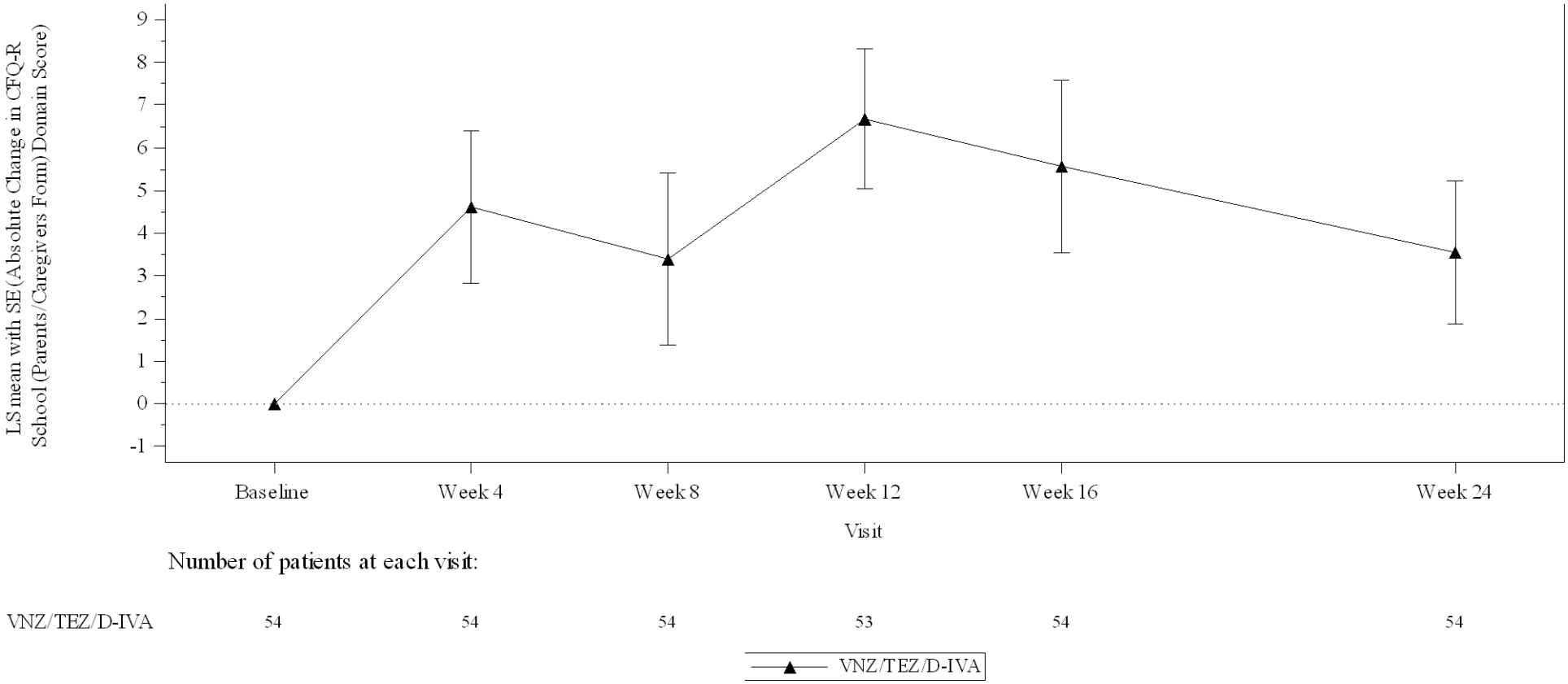
Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-nonfmf.sas Creation: 06FEB2025 10:17

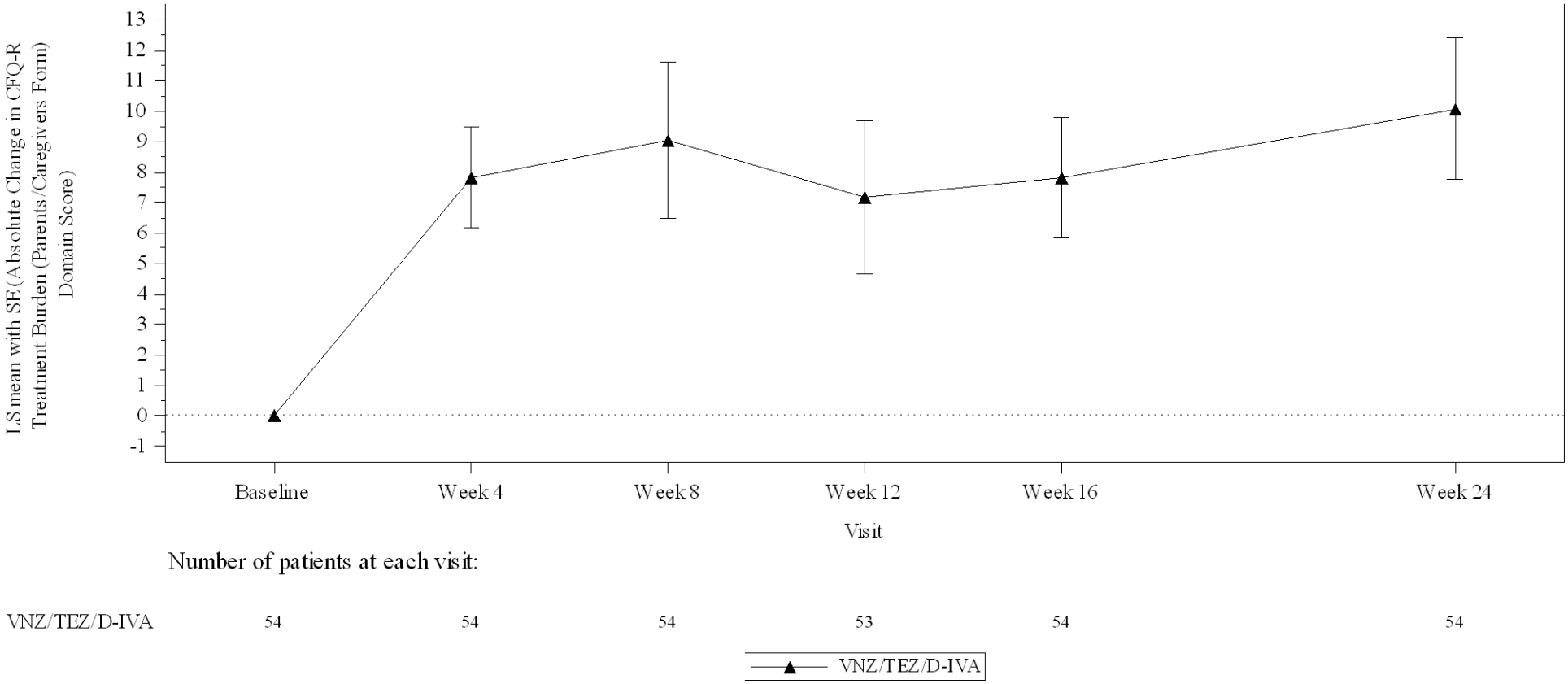
Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: School (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-nonfmf.sas Creation: 06FEB2025 10:17

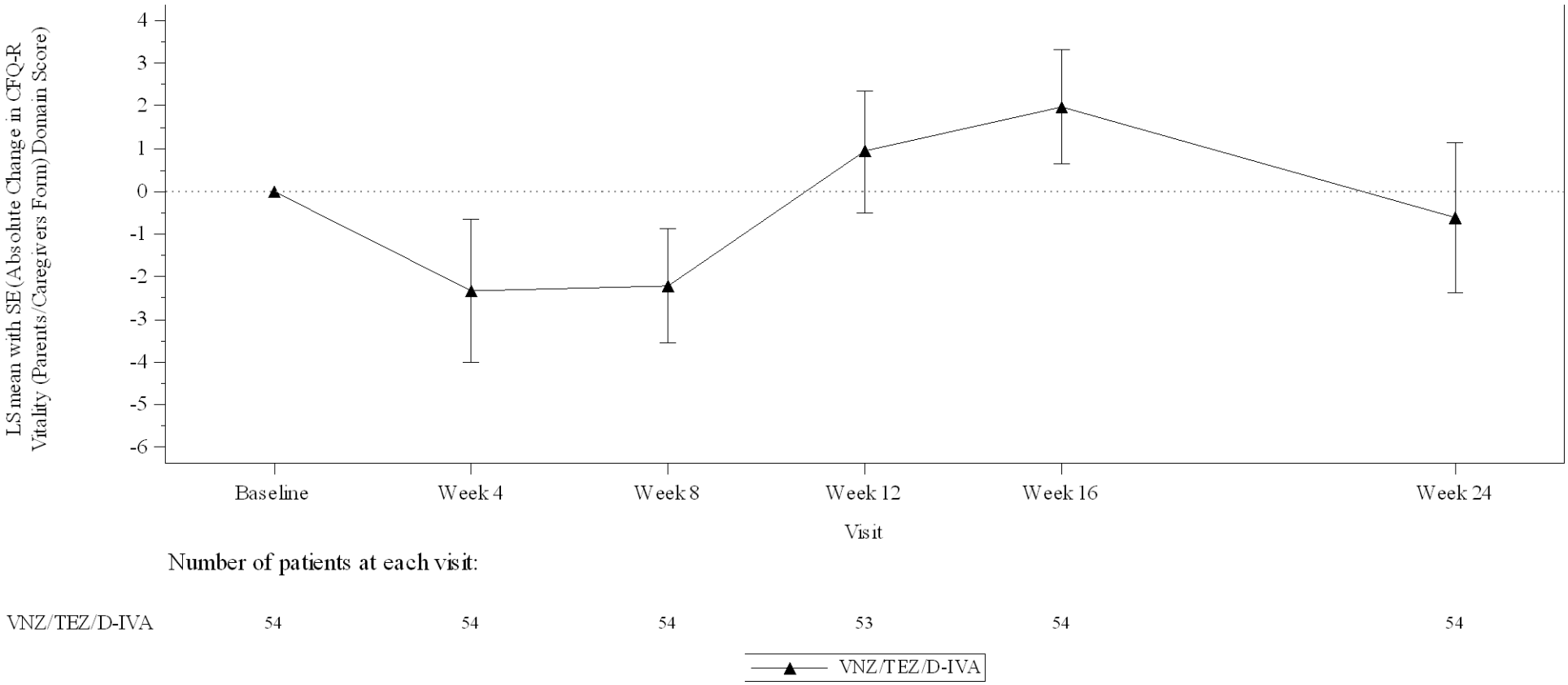
Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-nonfmf.sas Creation: 06FEB2025 10:17

Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

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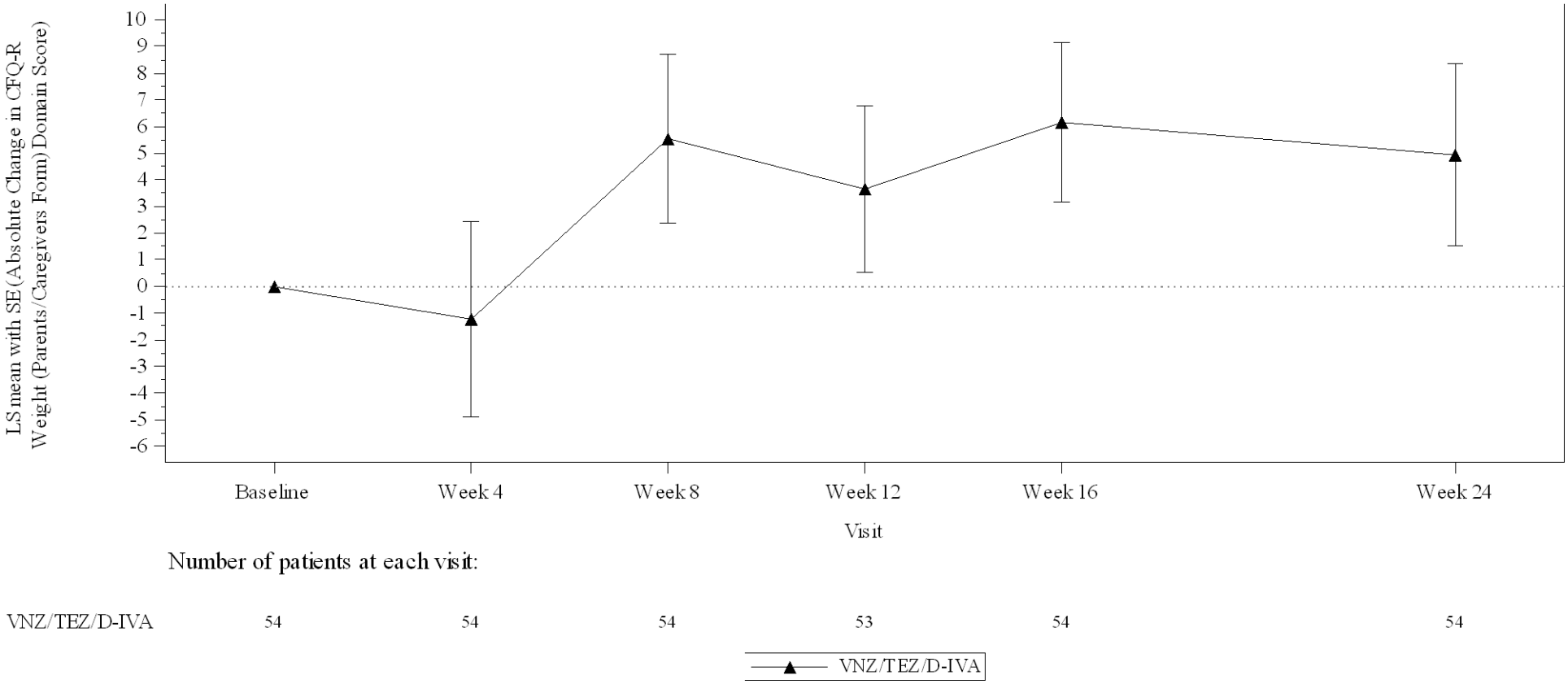
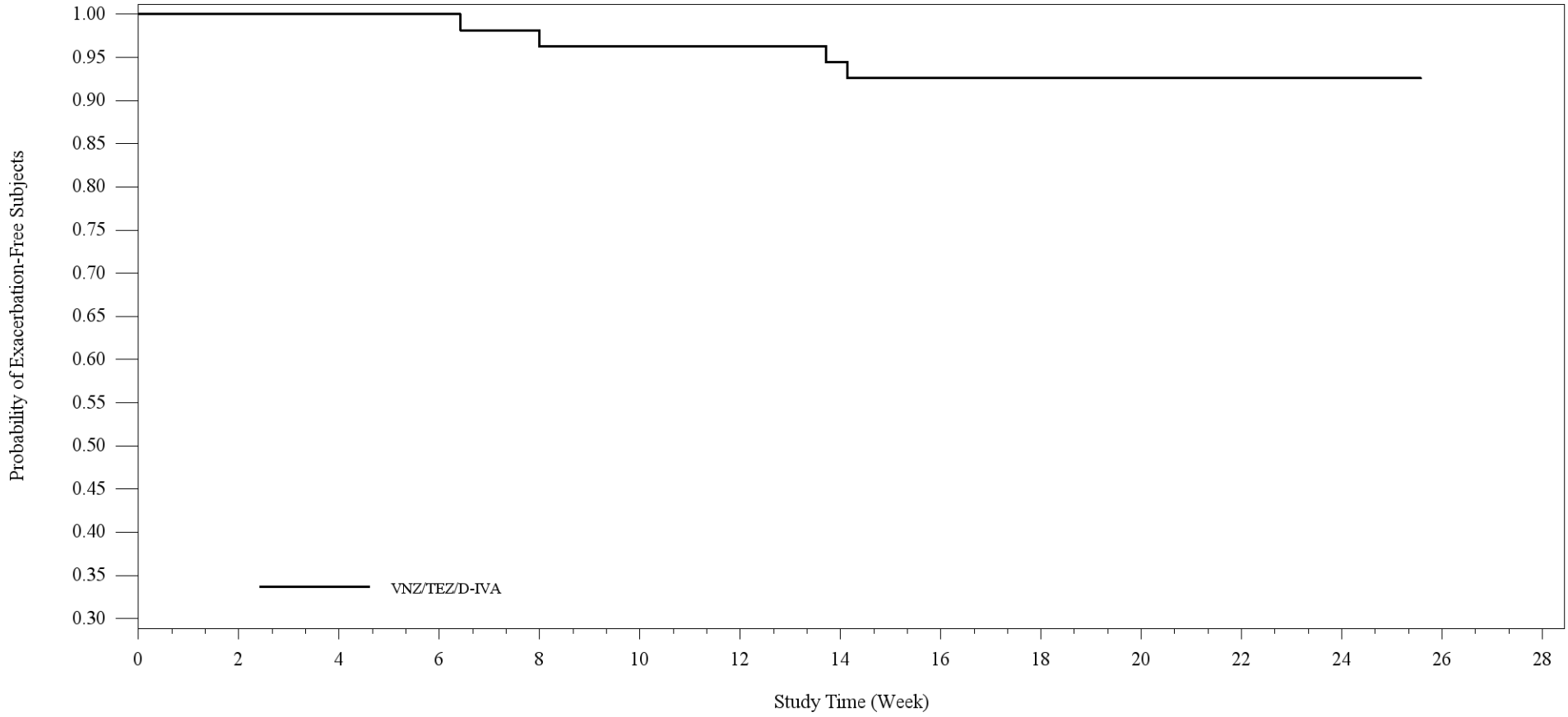
Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1-nonfmf.sas Creation: 06FEB2025 10:17

Figure 2.2.1.14.2
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 24 non-(F/MF)
Full Analysis Set

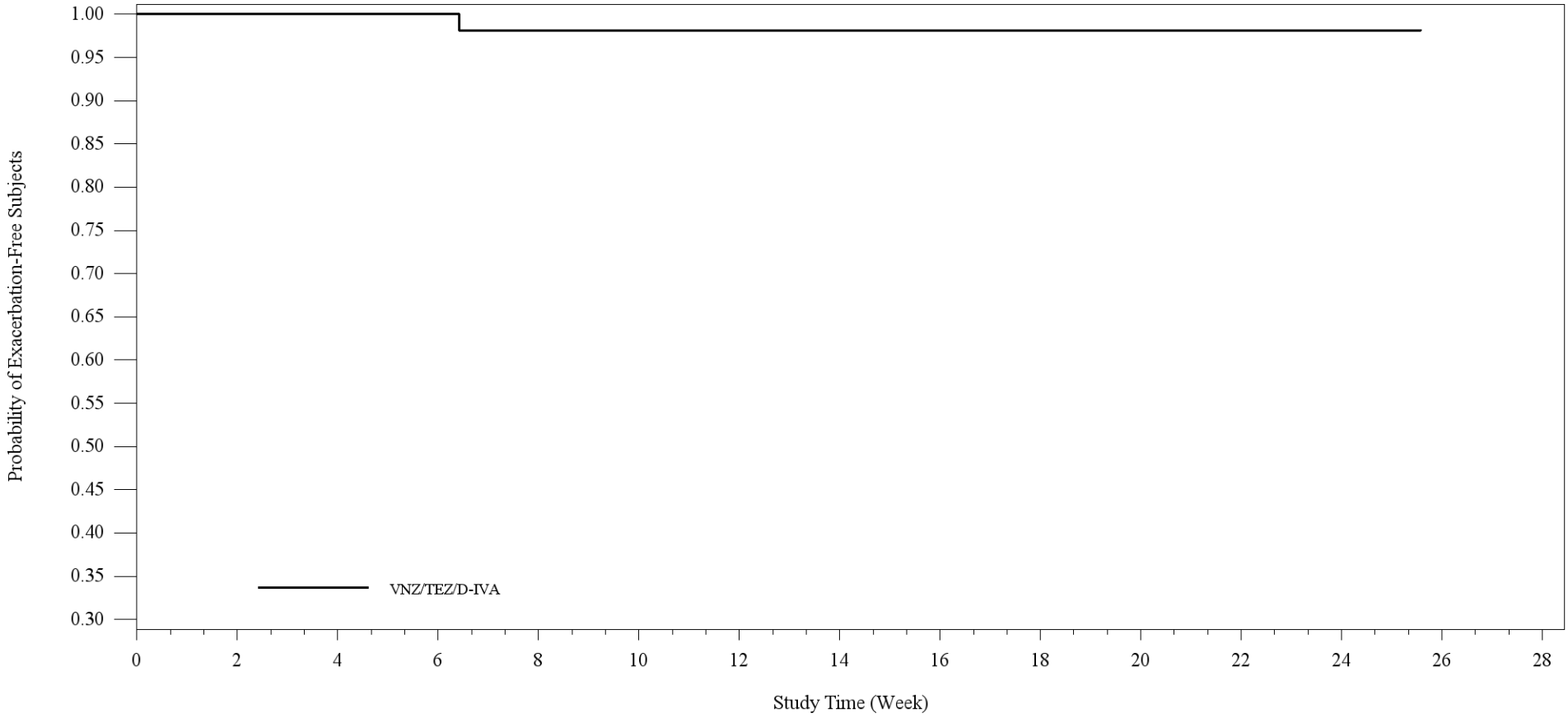


Number of Patients at Risk

VNZ/TEZ/D-IVA	54	54	52	52	50	31

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 2.2.1.15.2
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 24 non-(F/MF)
Full Analysis Set



Number of Patients at Risk

VNZ/TEZ/D-IVA	54	54	53	53	53	34

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- The PEx analysis period will include the time from the first dose date of study drug until the last efficacy assessment, which may be collected up to the Week 24 Visit or the earlier of Day 169 and the end of study participation if the subject does not have the Week 24 Visit.

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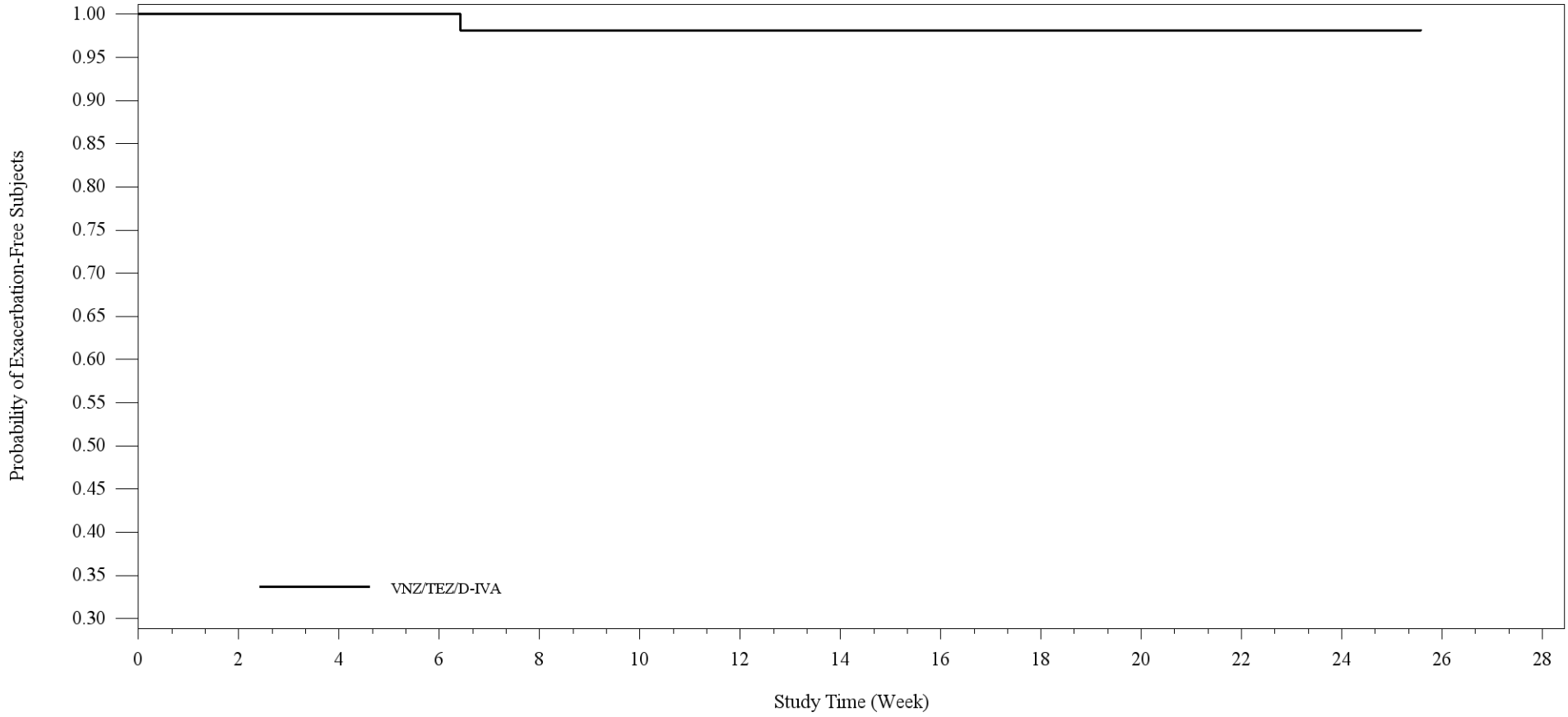
Figure 2.2.1.16.2
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics through Week 24 non-(F/MF)
Full Analysis Set

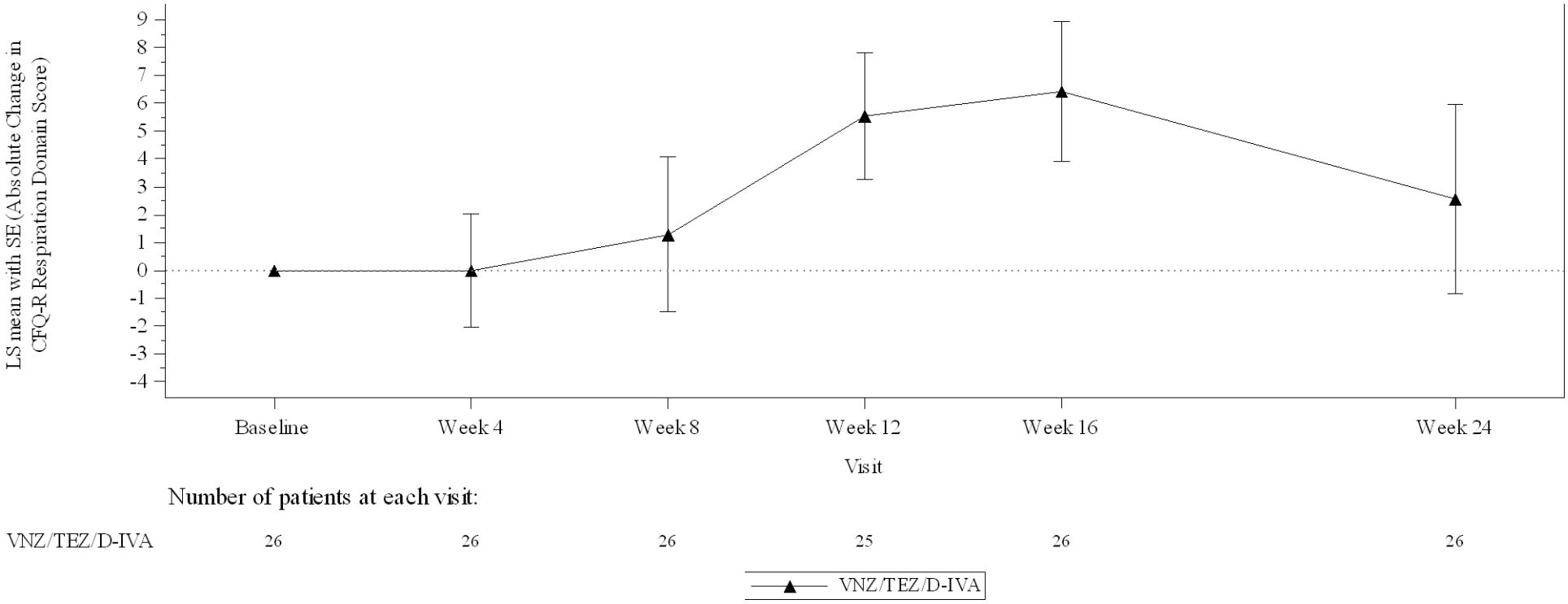


Number of Patients at Risk

VNZ/TEZ/D-IVA	54	54	53	53	53	34

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

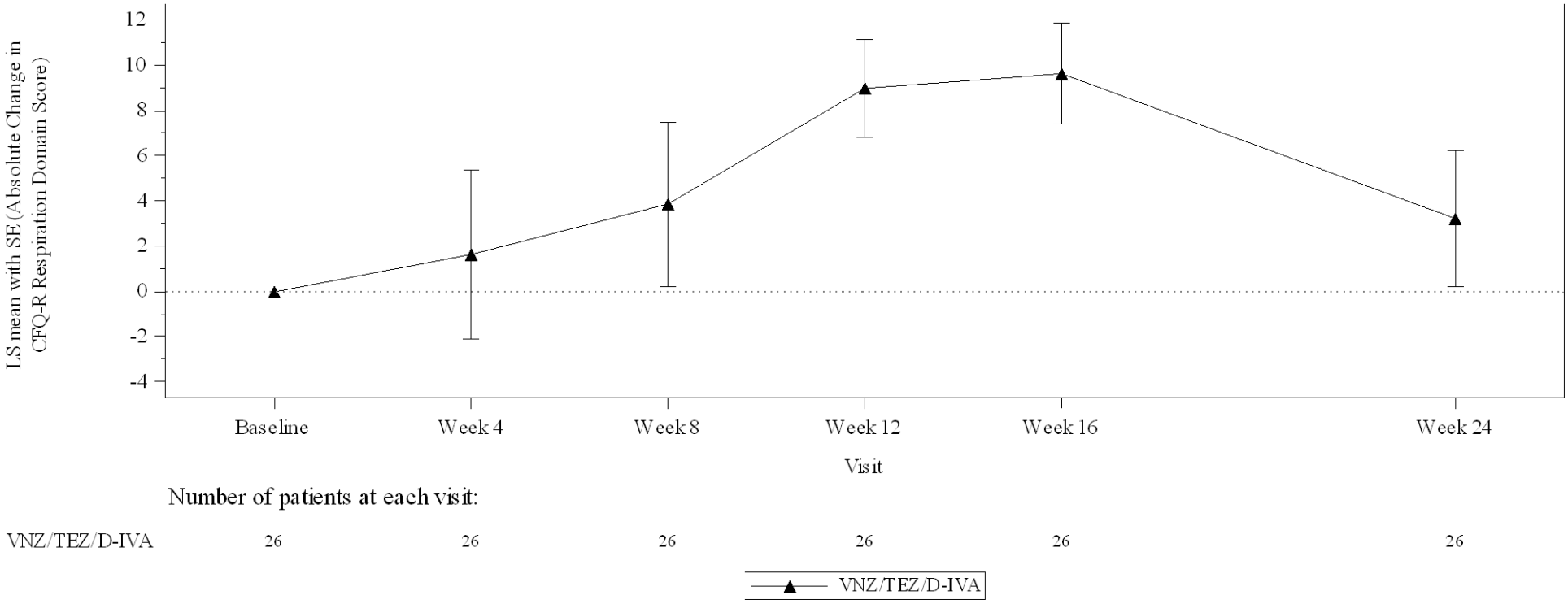
Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

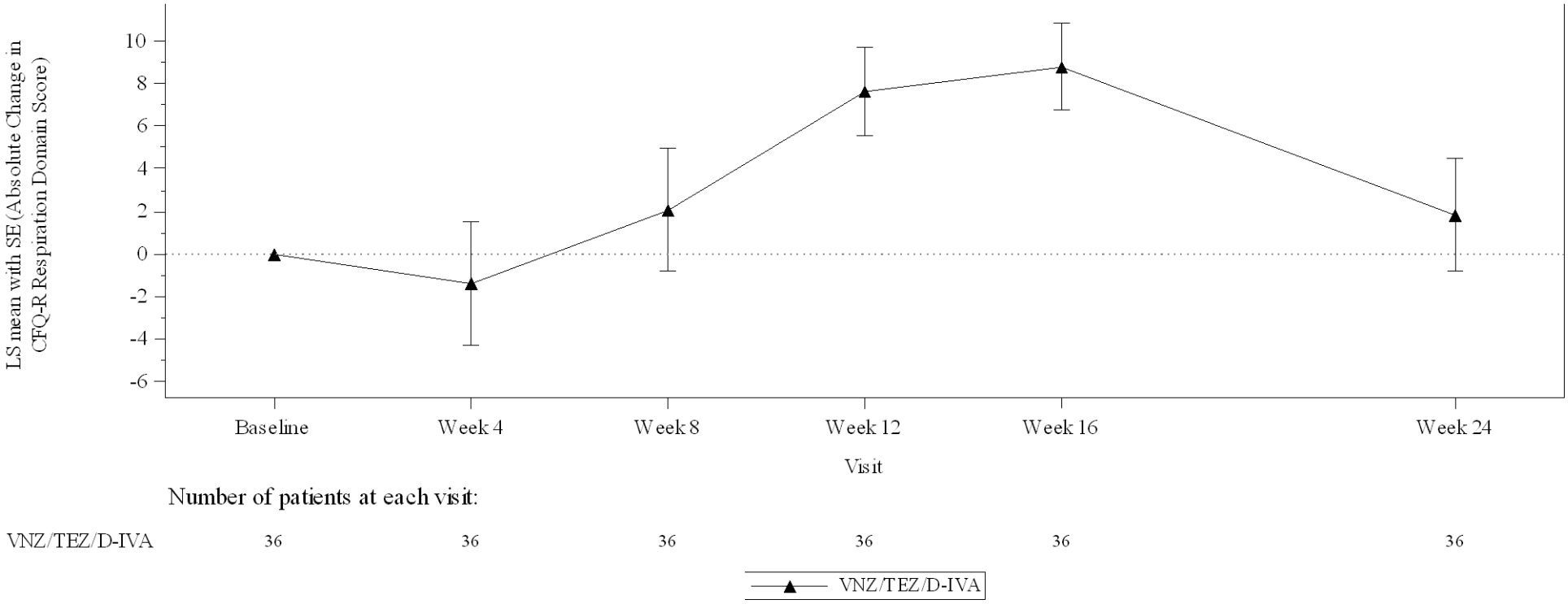
Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

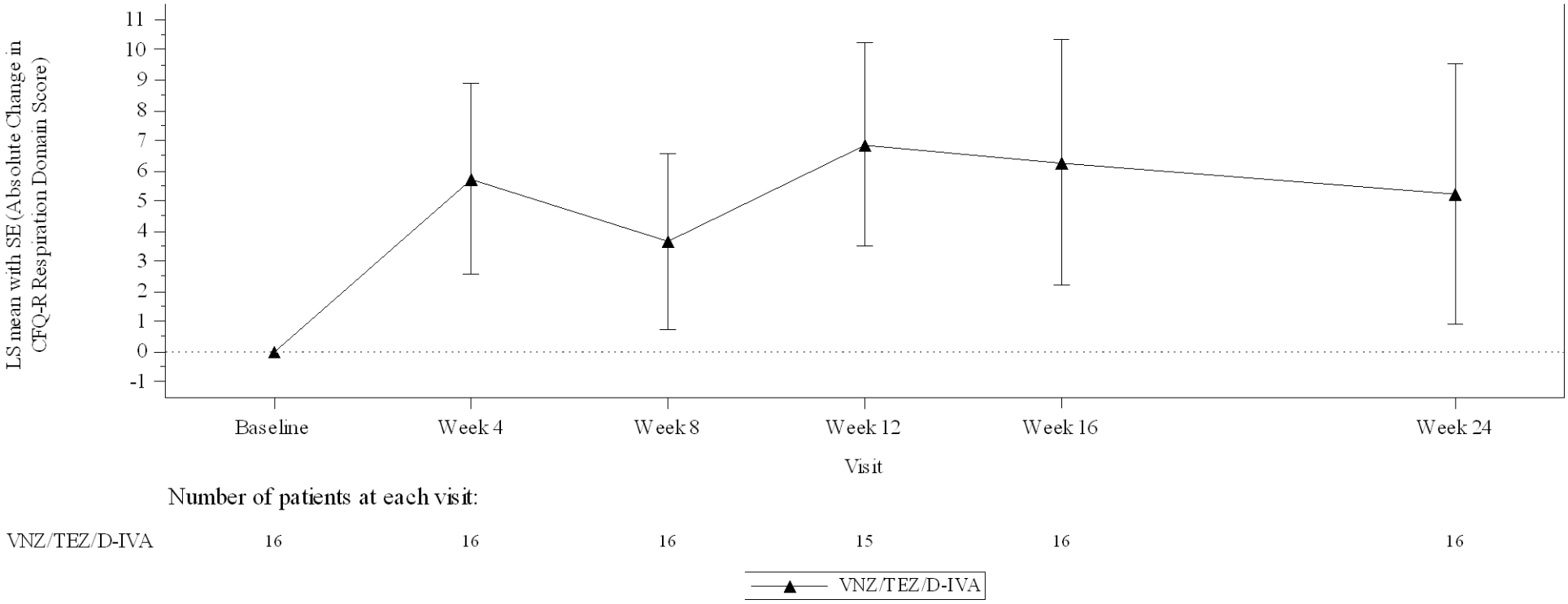
Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

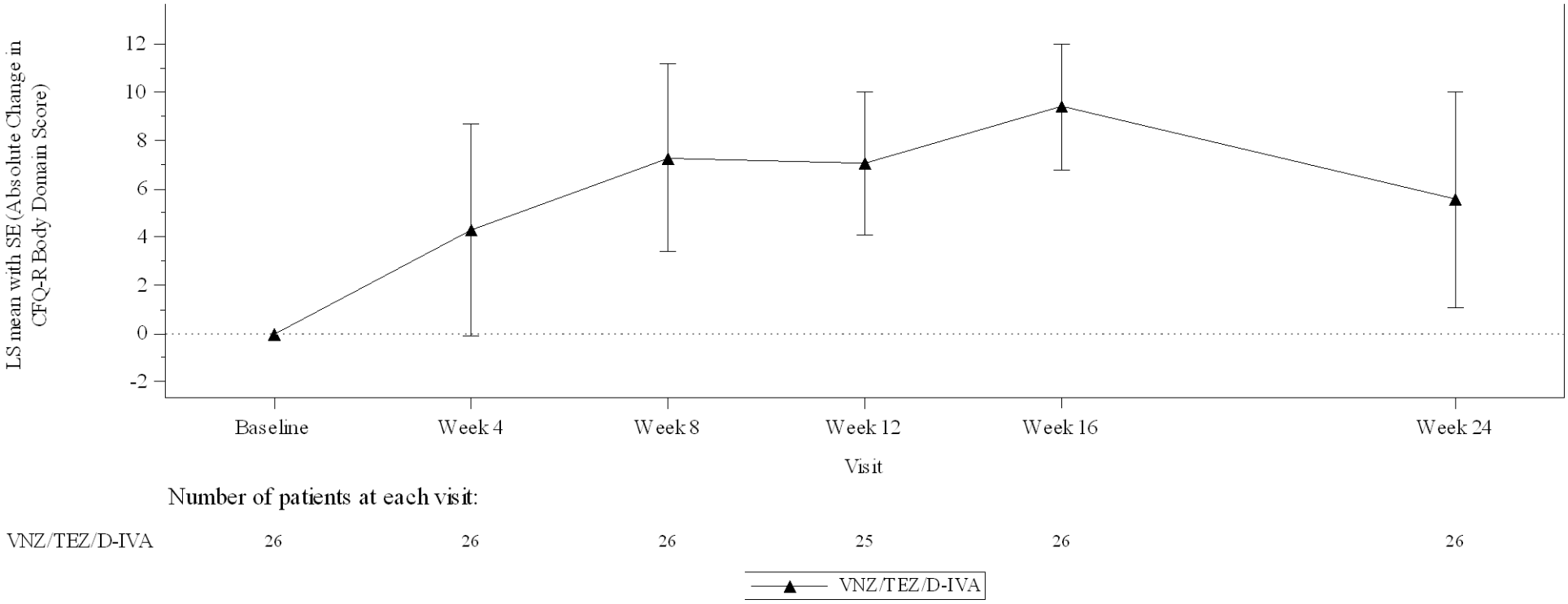
Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

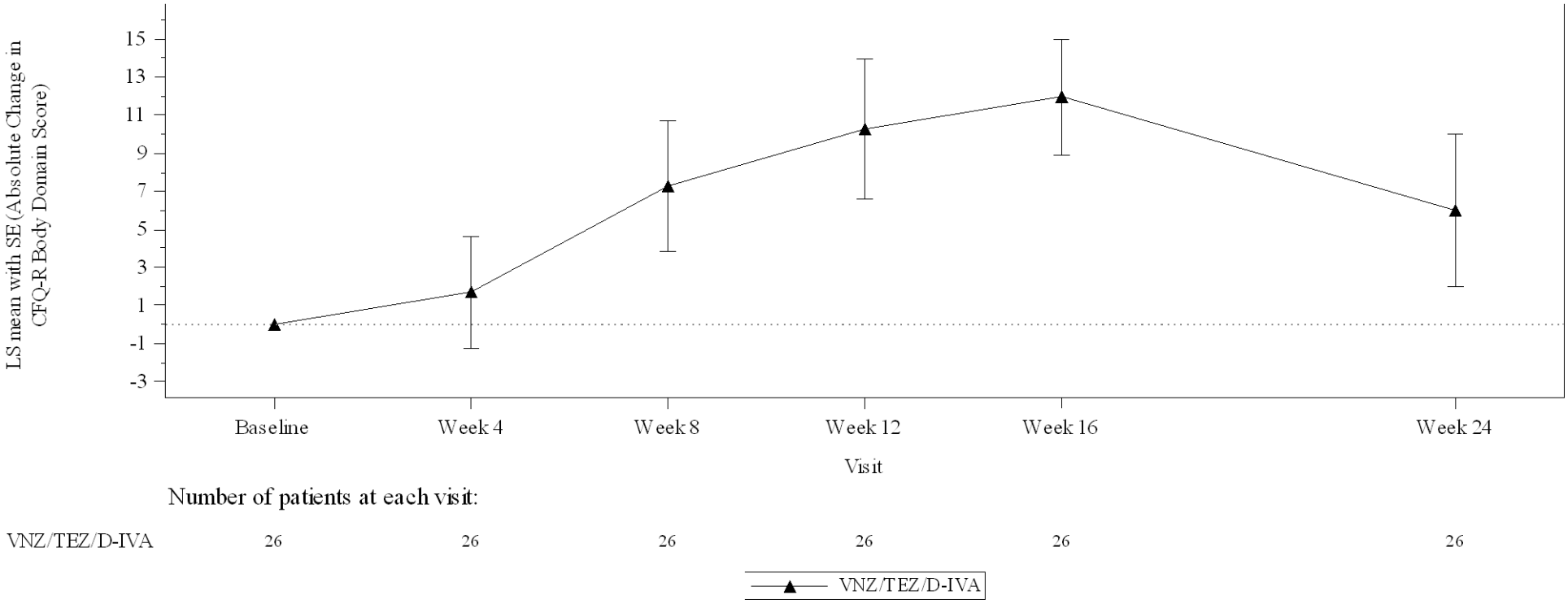
Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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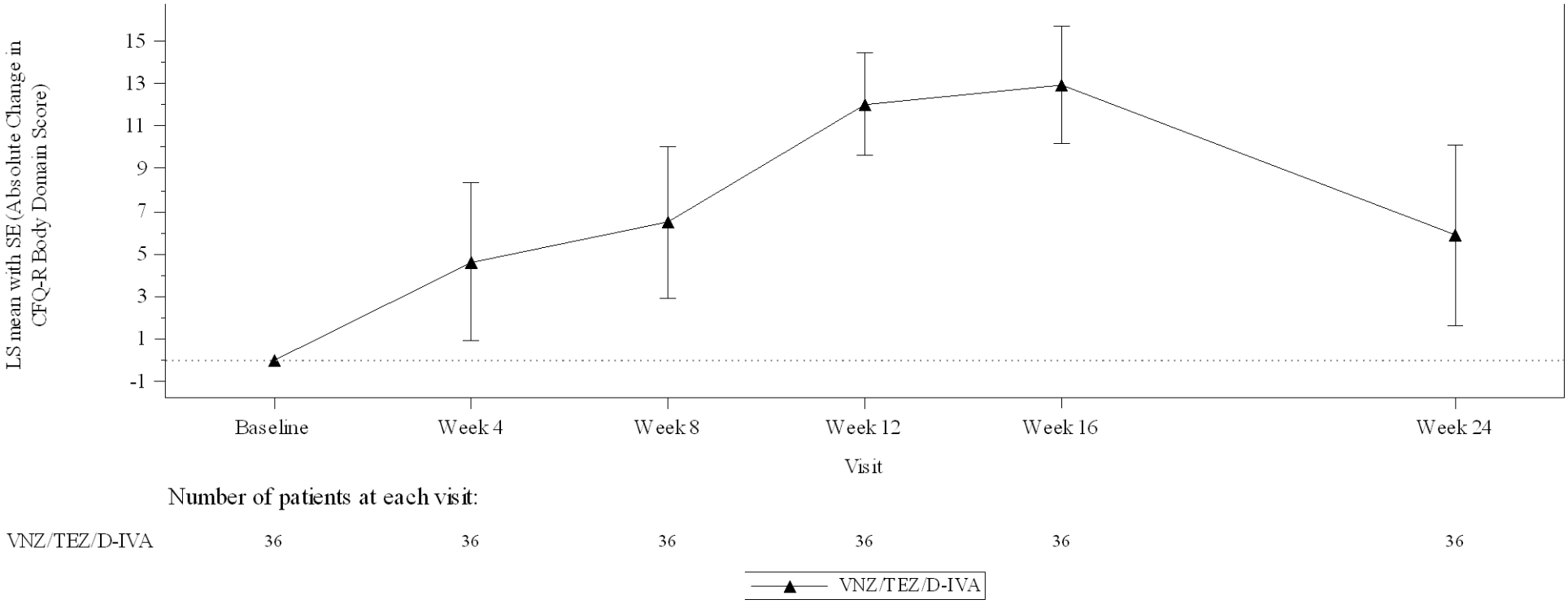
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body
Region = North America



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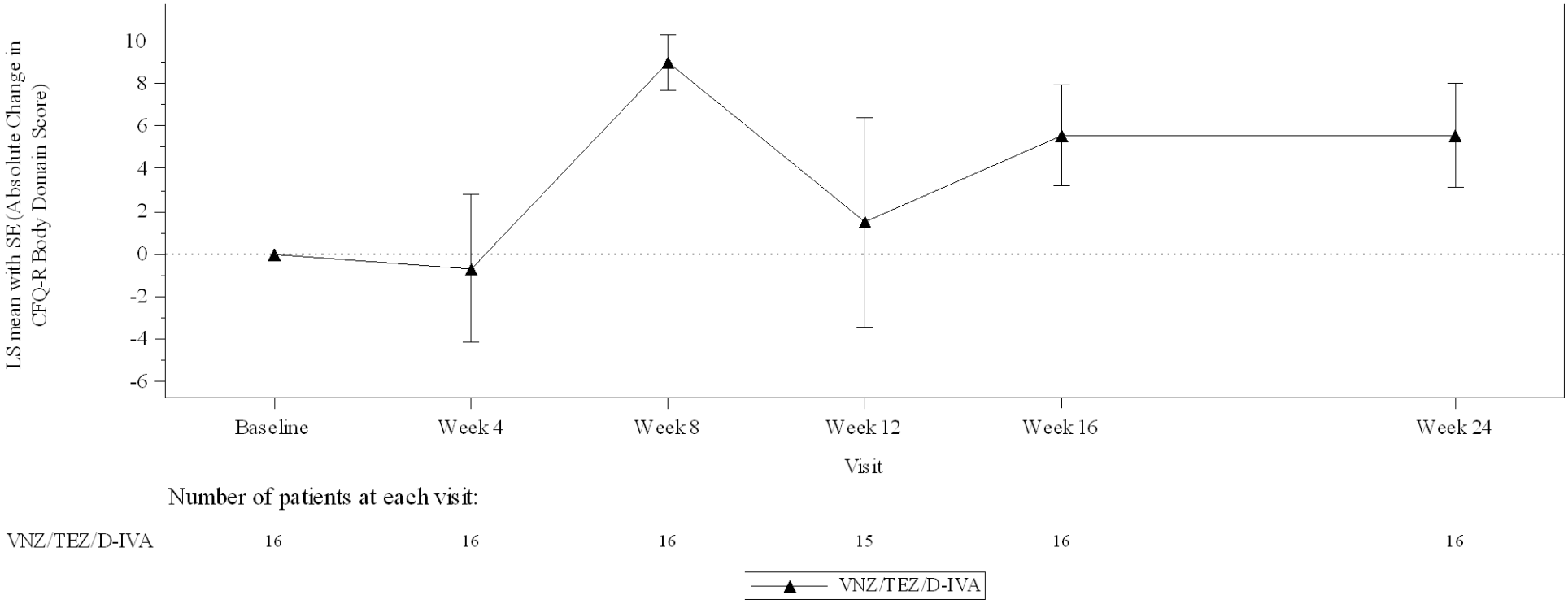
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

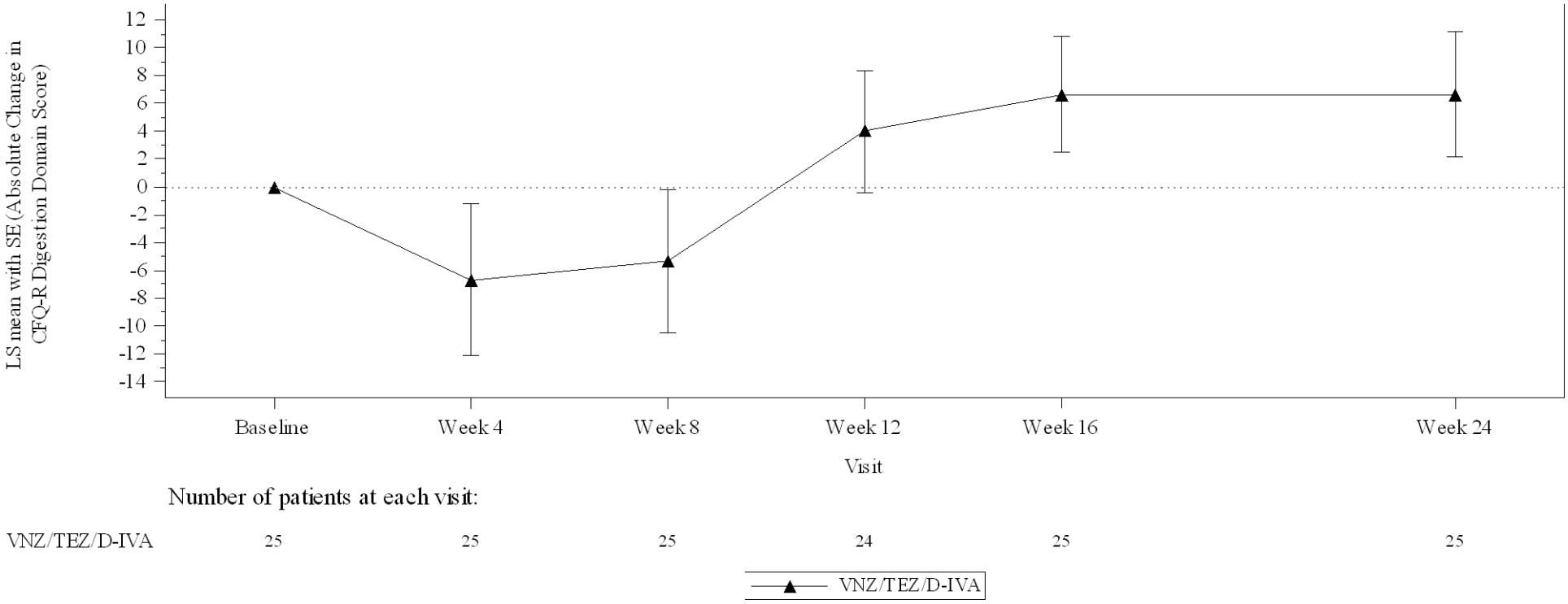
Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion
Sex = Male



Number of patients at each visit:

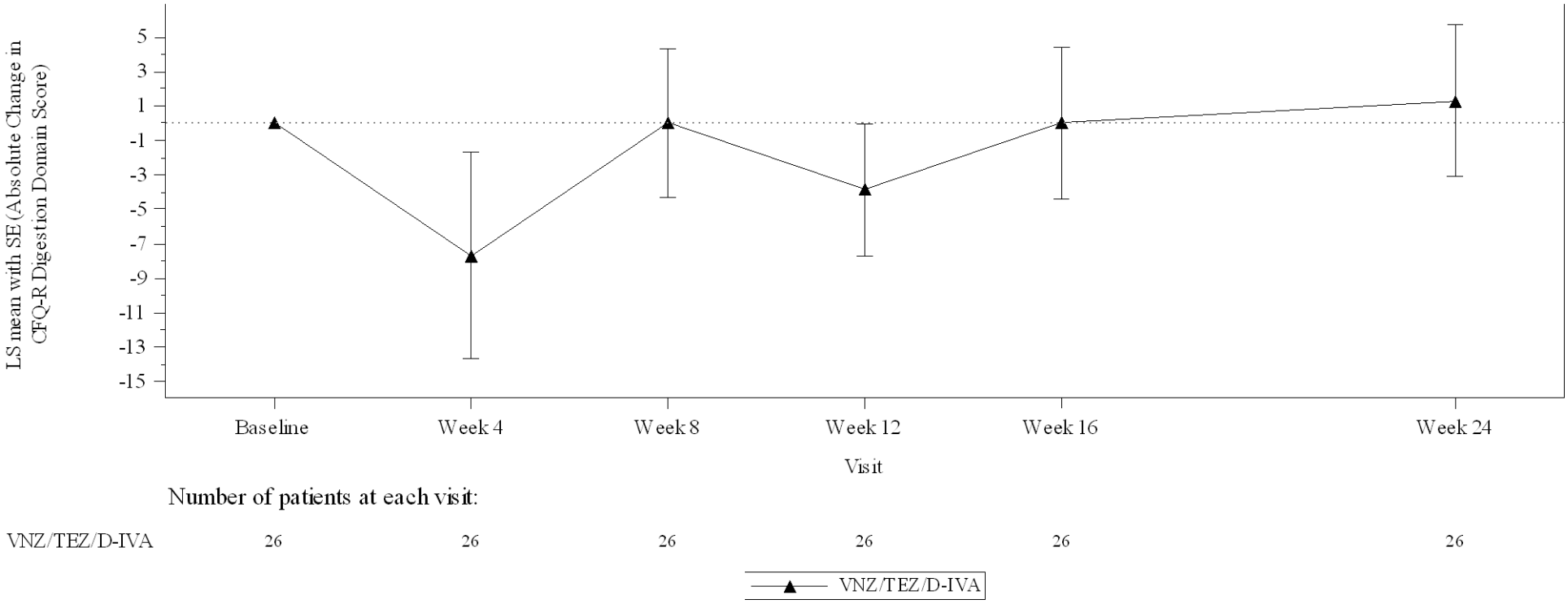
VNZ/TEZ/D-IVA	25	25	25	24	25	25

VNZ/TEZ/D-IVA

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion
Sex = Female



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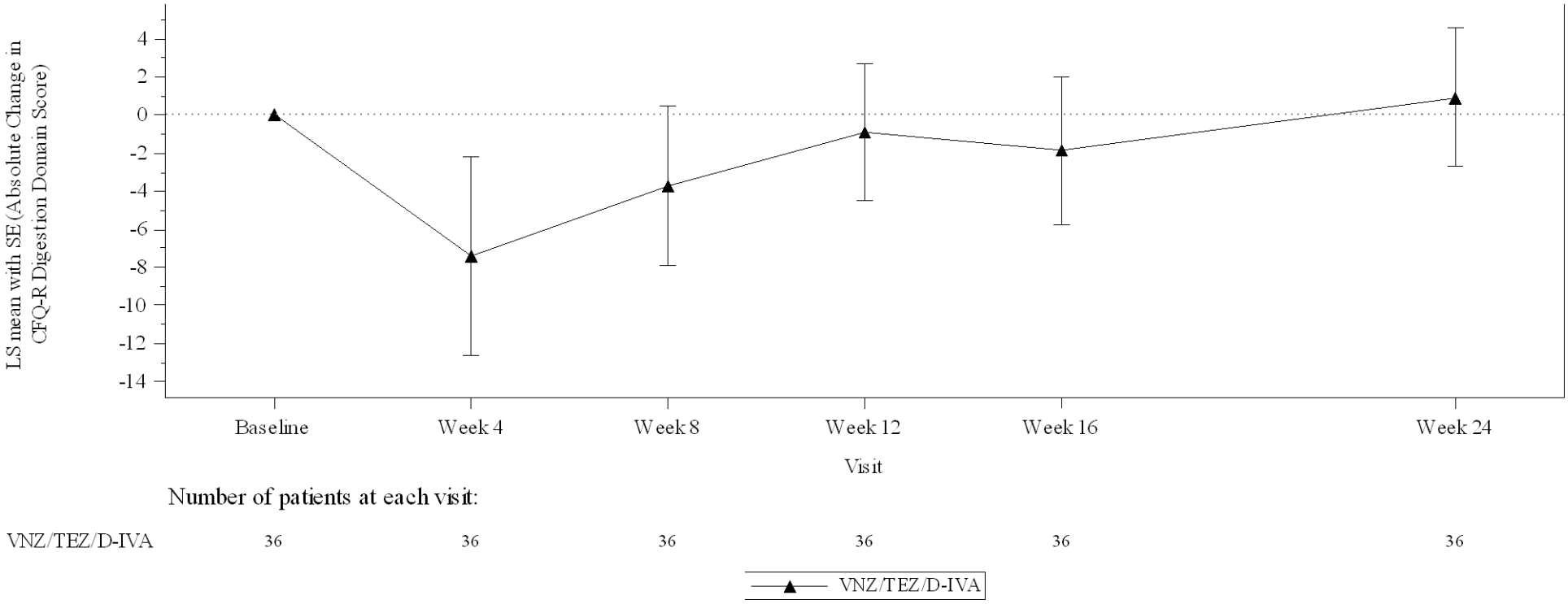
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion
Region = North America



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- Baseline is defined as the pre-dose Day 1 value.
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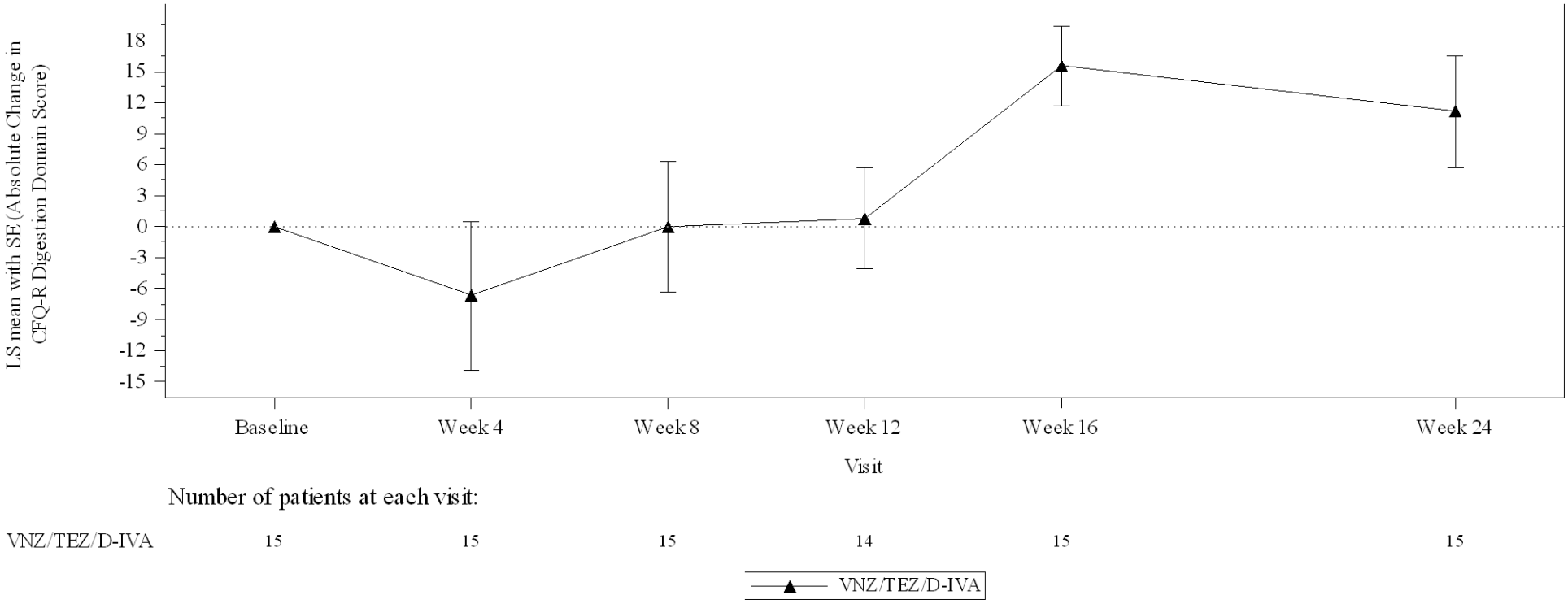
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion
Region = Rest of World



Number of patients at each visit:

	Baseline	Week 4	Week 8	Week 12	Week 16	Week 24
VNZ/TEZ/D-IVA	15	15	15	14	15	15

VNZ/TEZ/D-IVA

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

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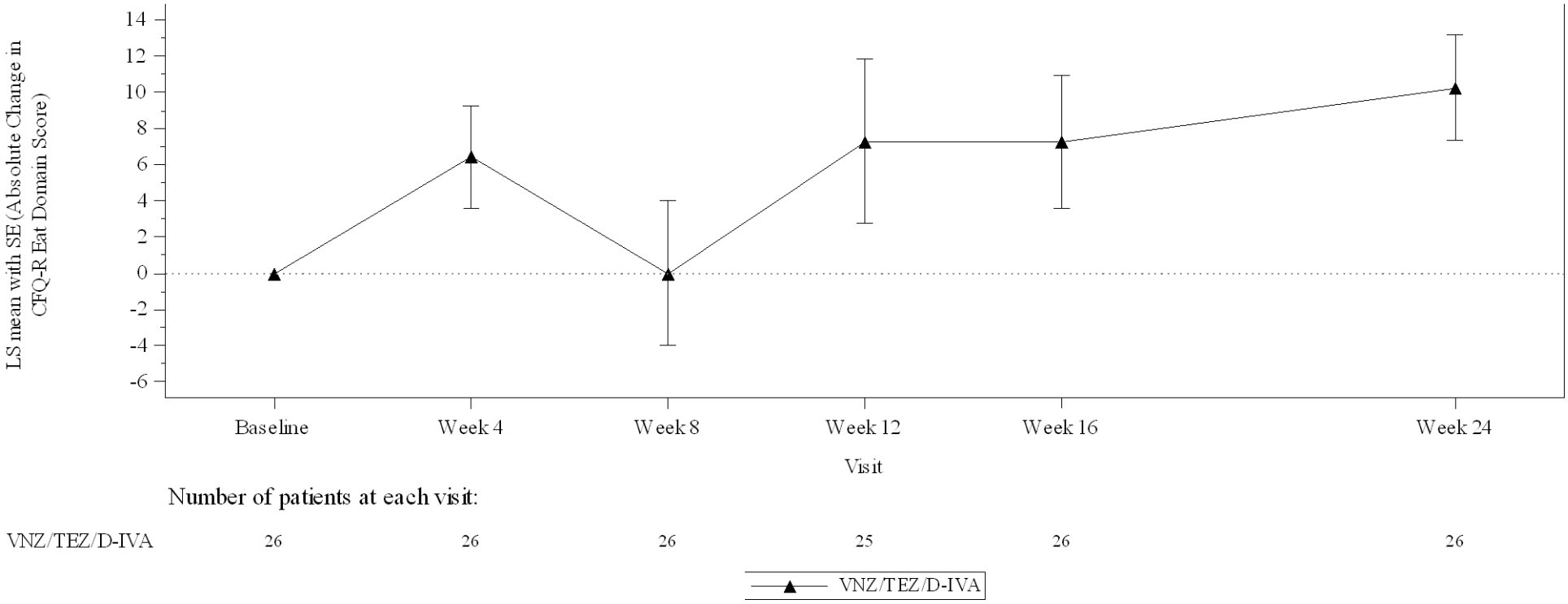
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat
Sex = Male



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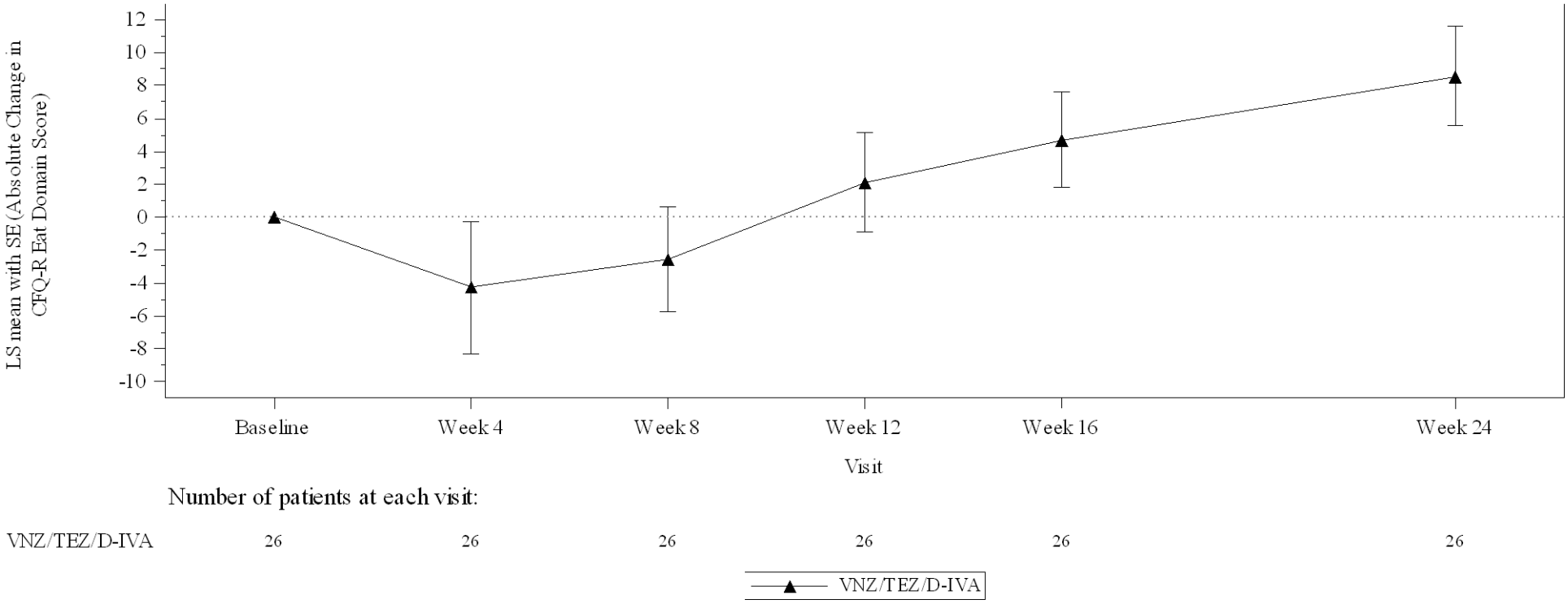
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat
Sex = Female



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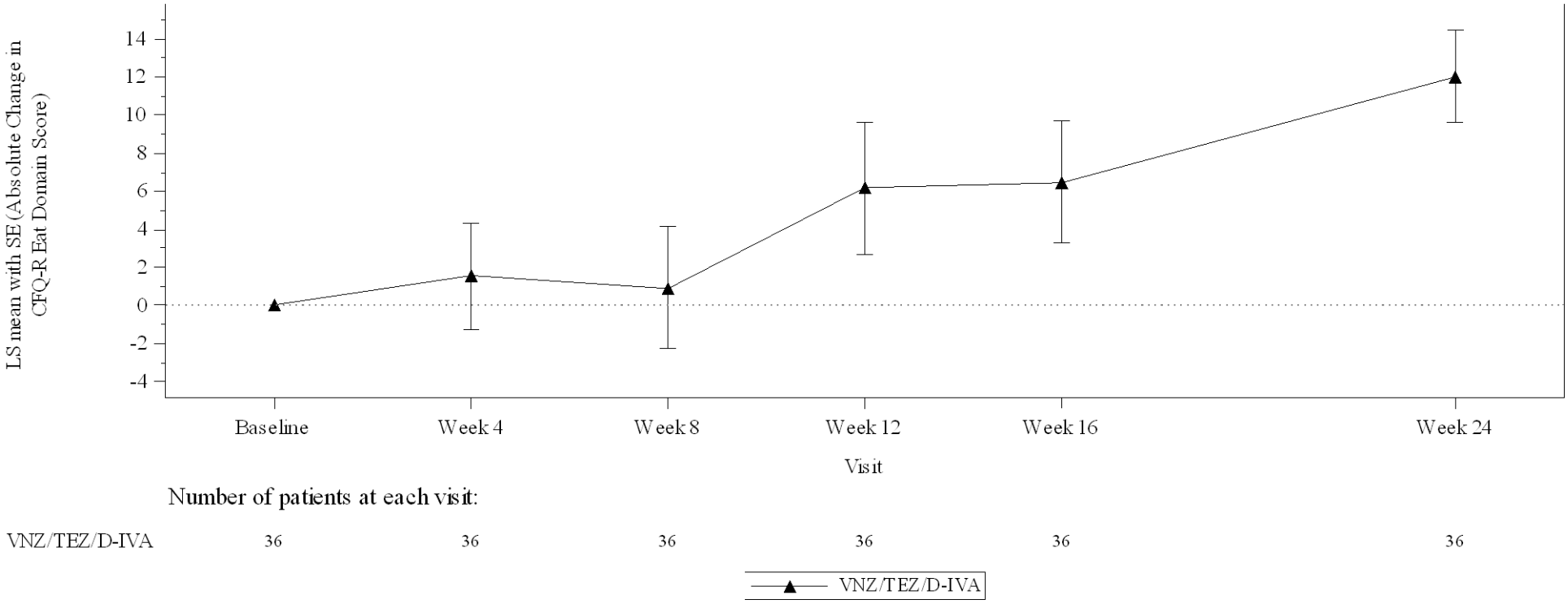
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat
Region = North America



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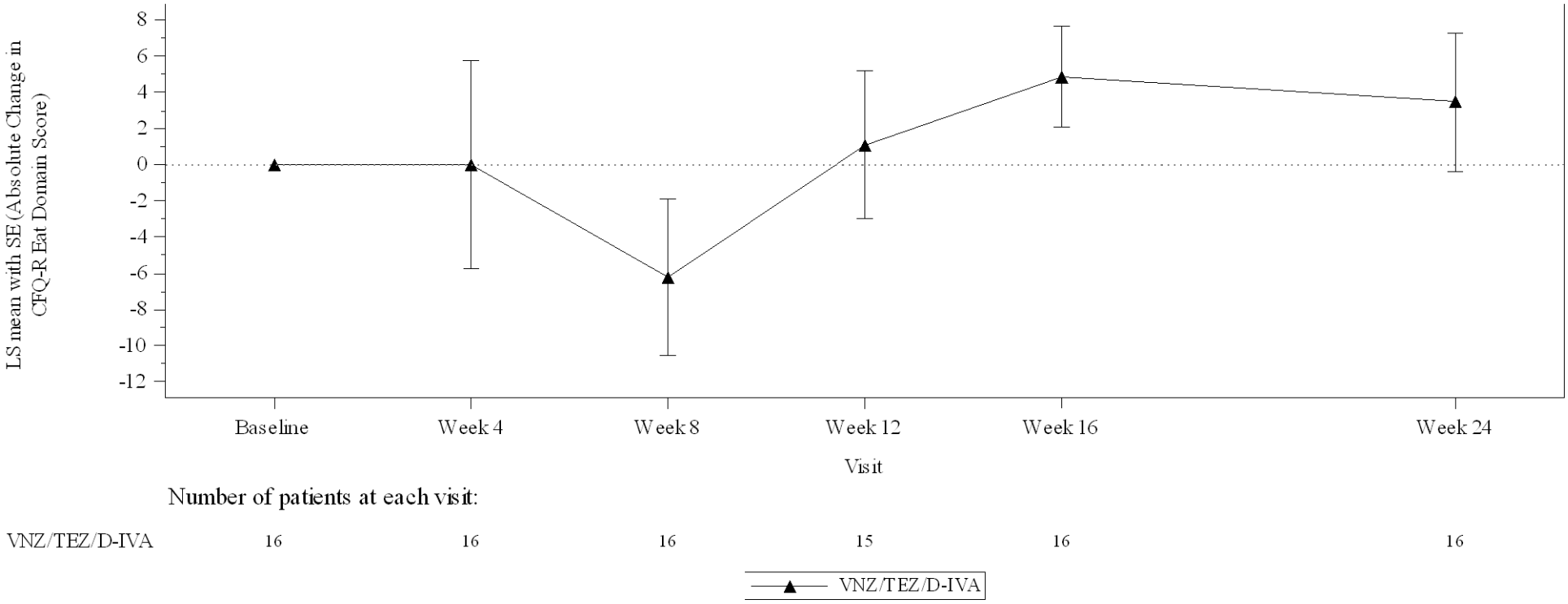
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat
Region = Rest of World



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- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

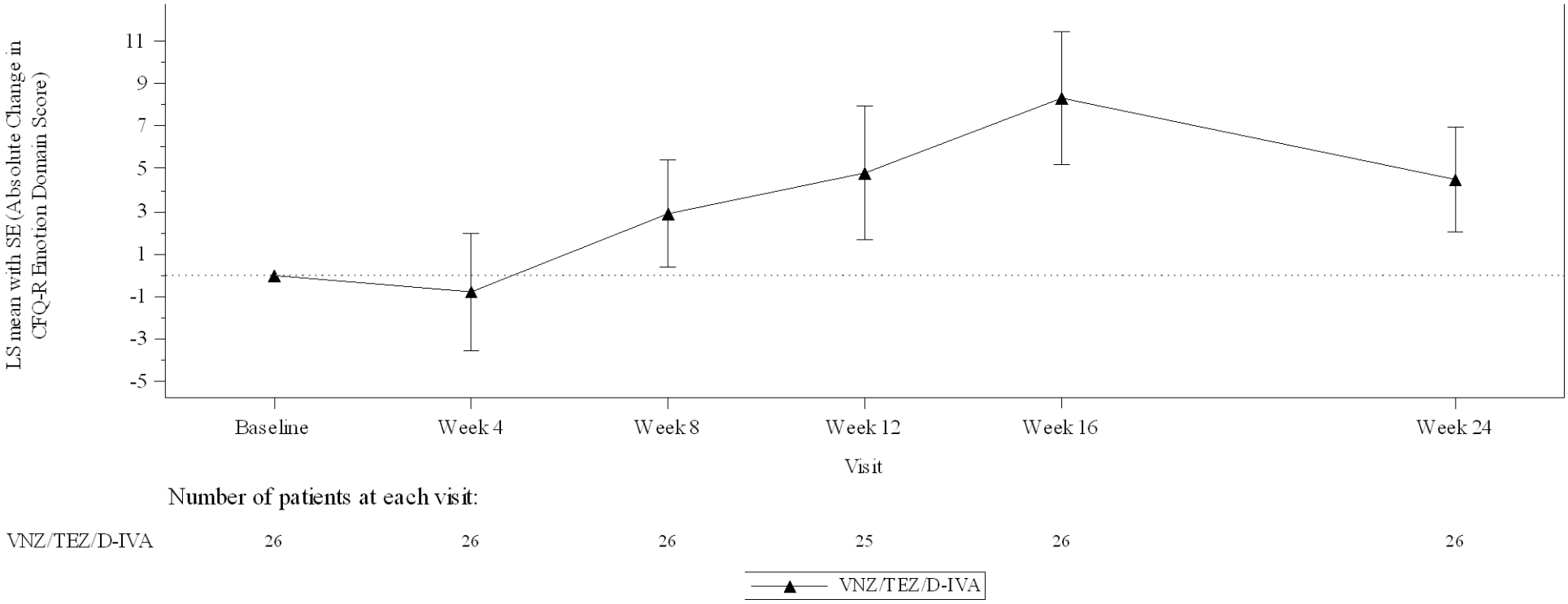
Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

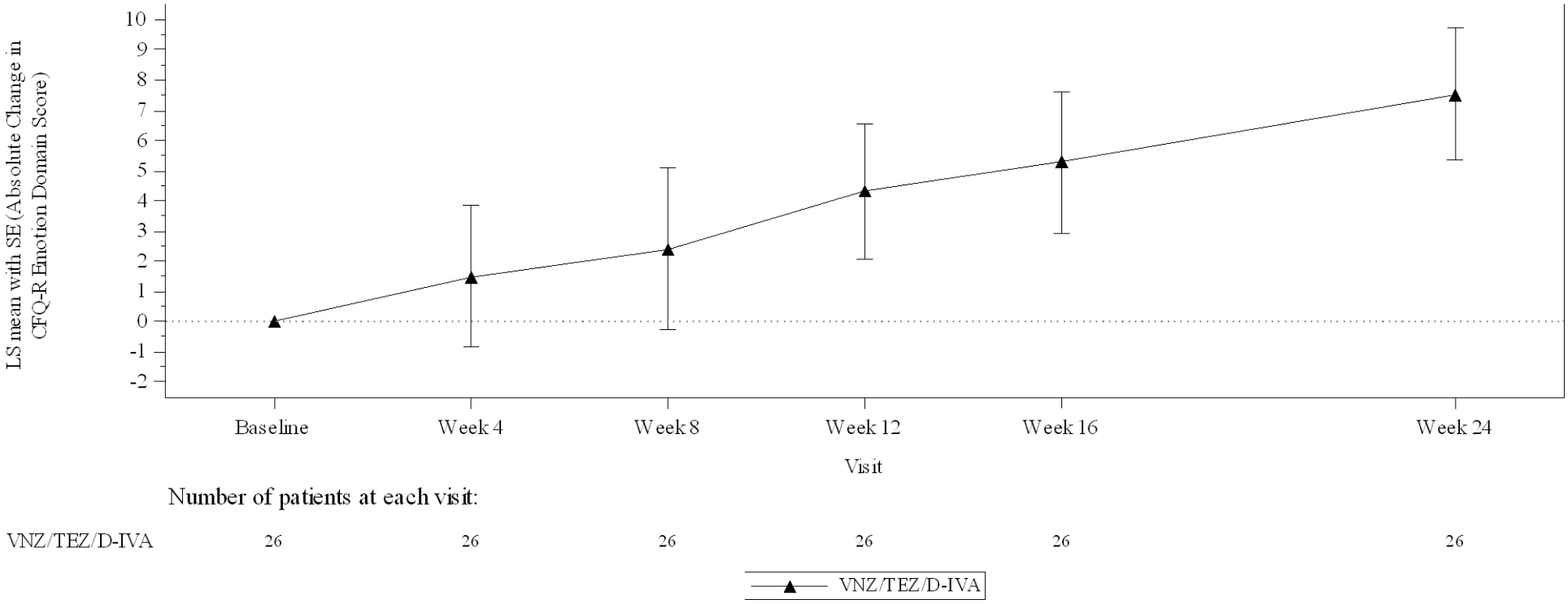
Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

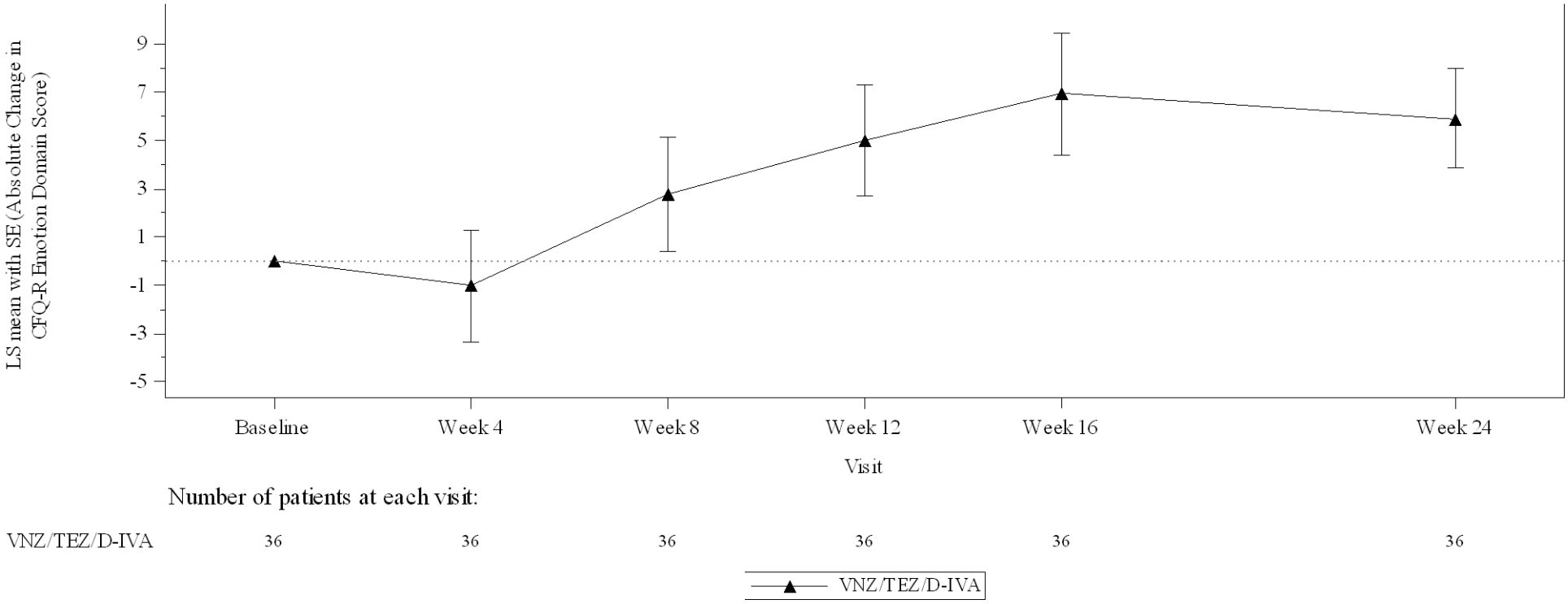
Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion
Region = North America



Number of patients at each visit:

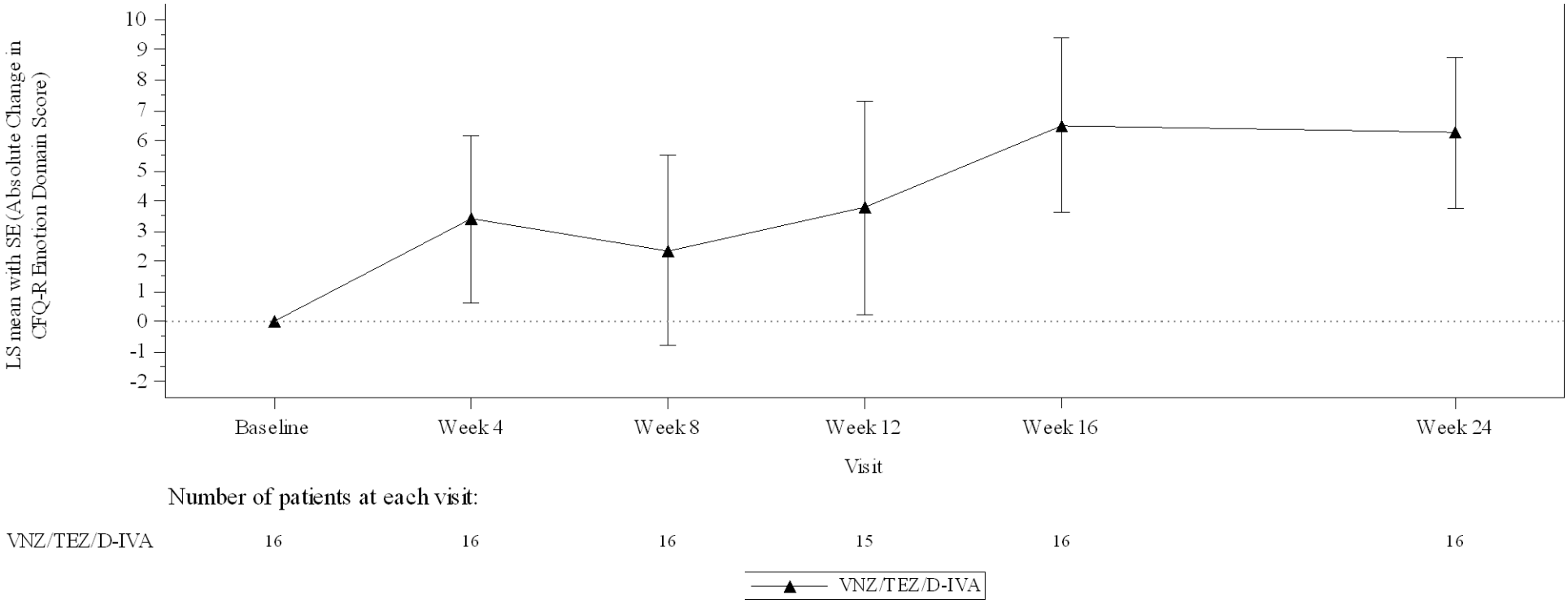
	Baseline	Week 4	Week 8	Week 12	Week 16	Week 24
VNZ/TEZ/D-IVA	36	36	36	36	36	36

VNZ/TEZ/D-IVA

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

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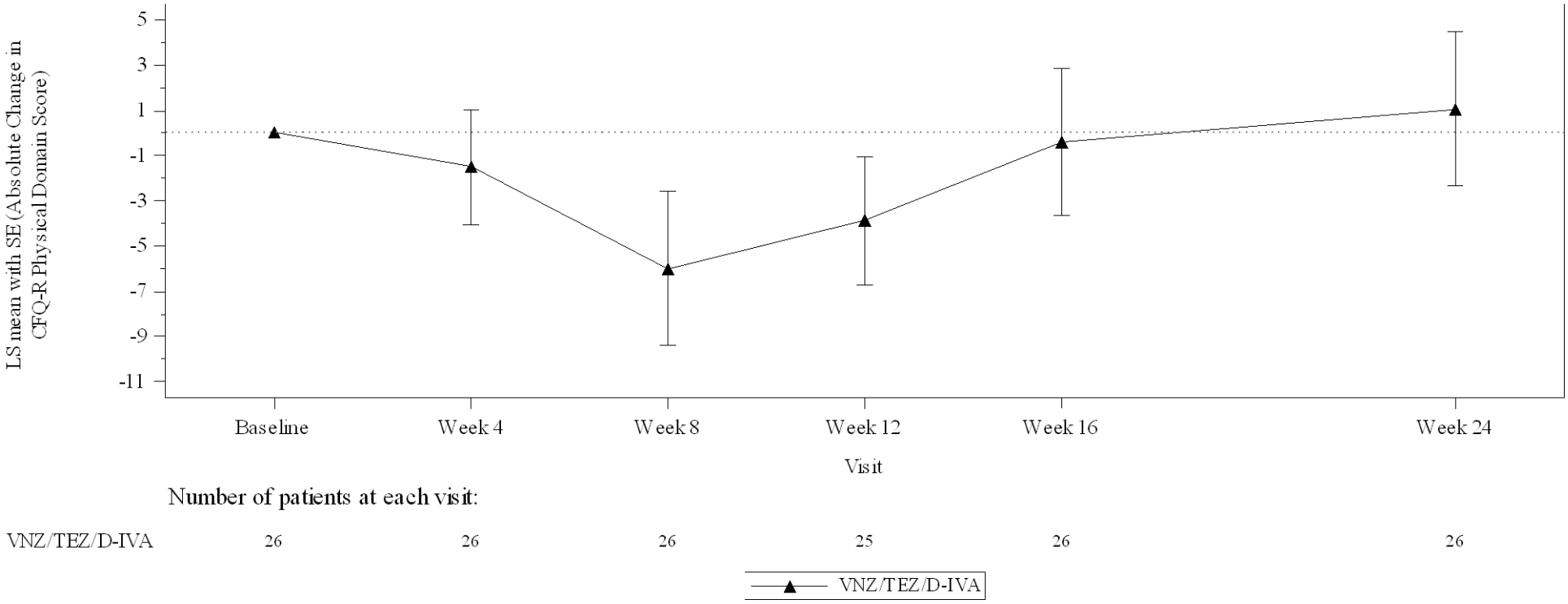
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

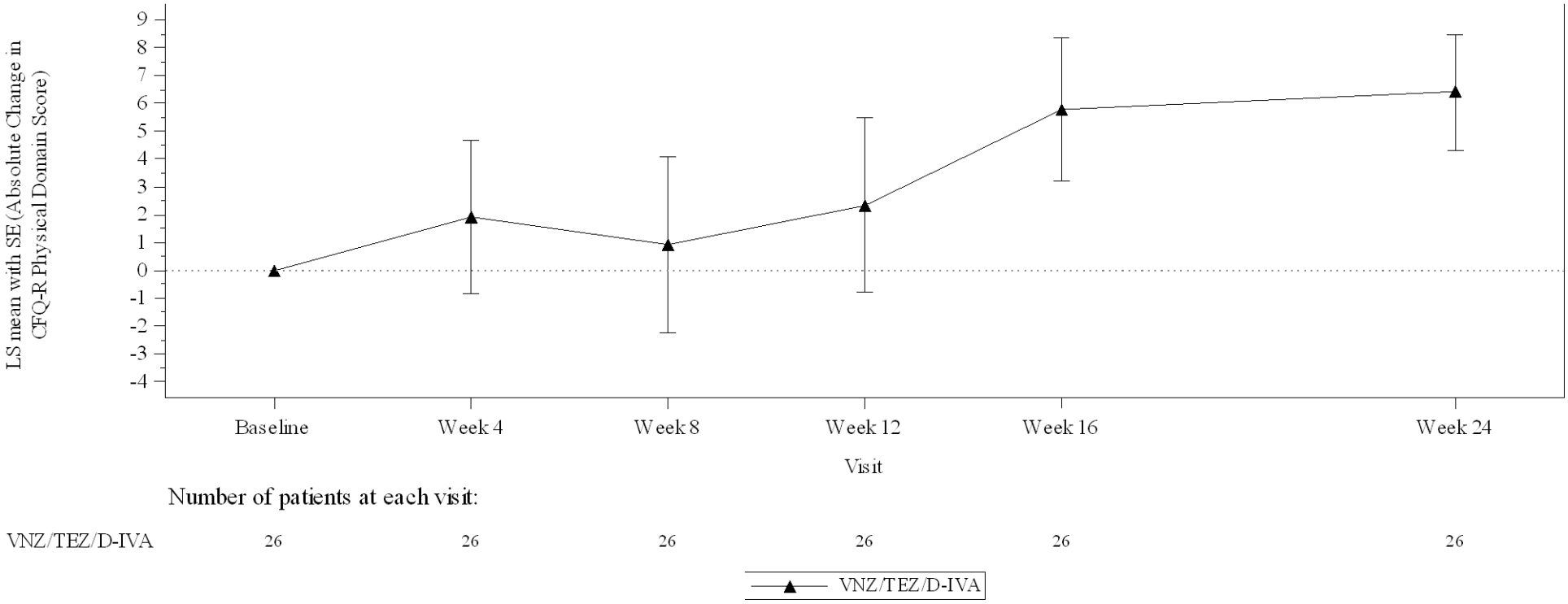
Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

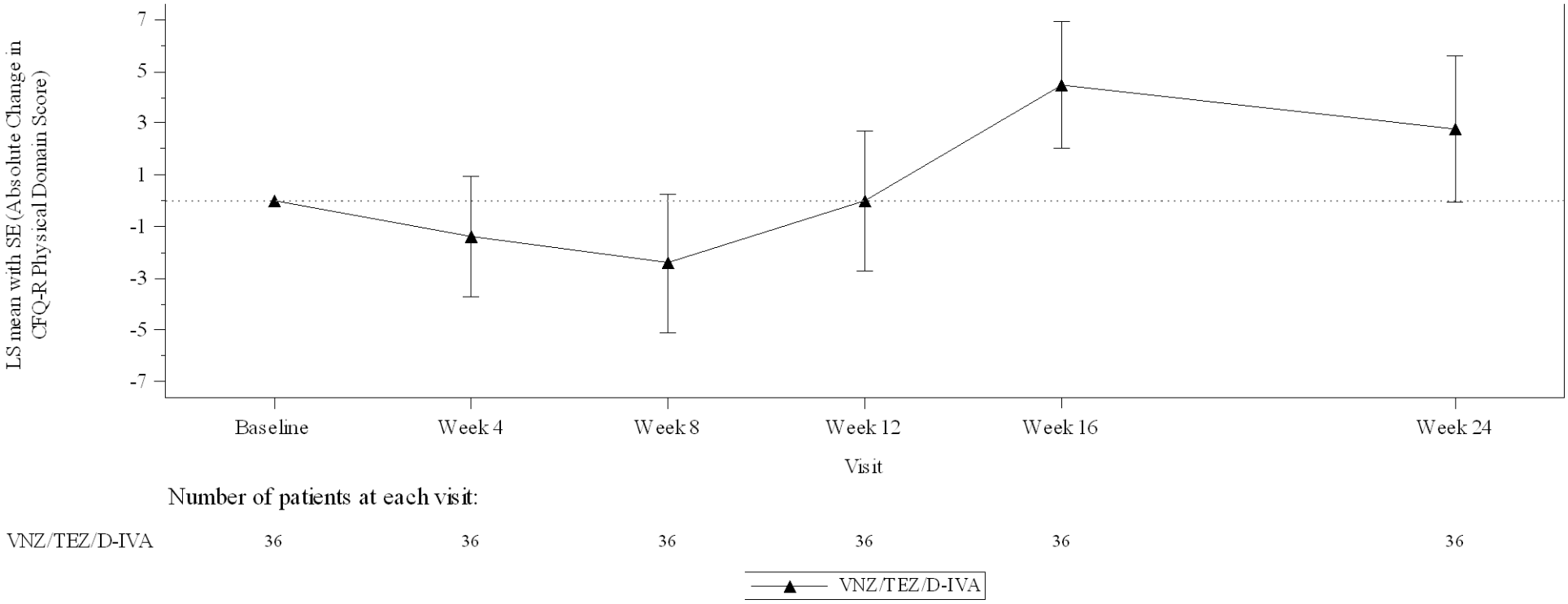
Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

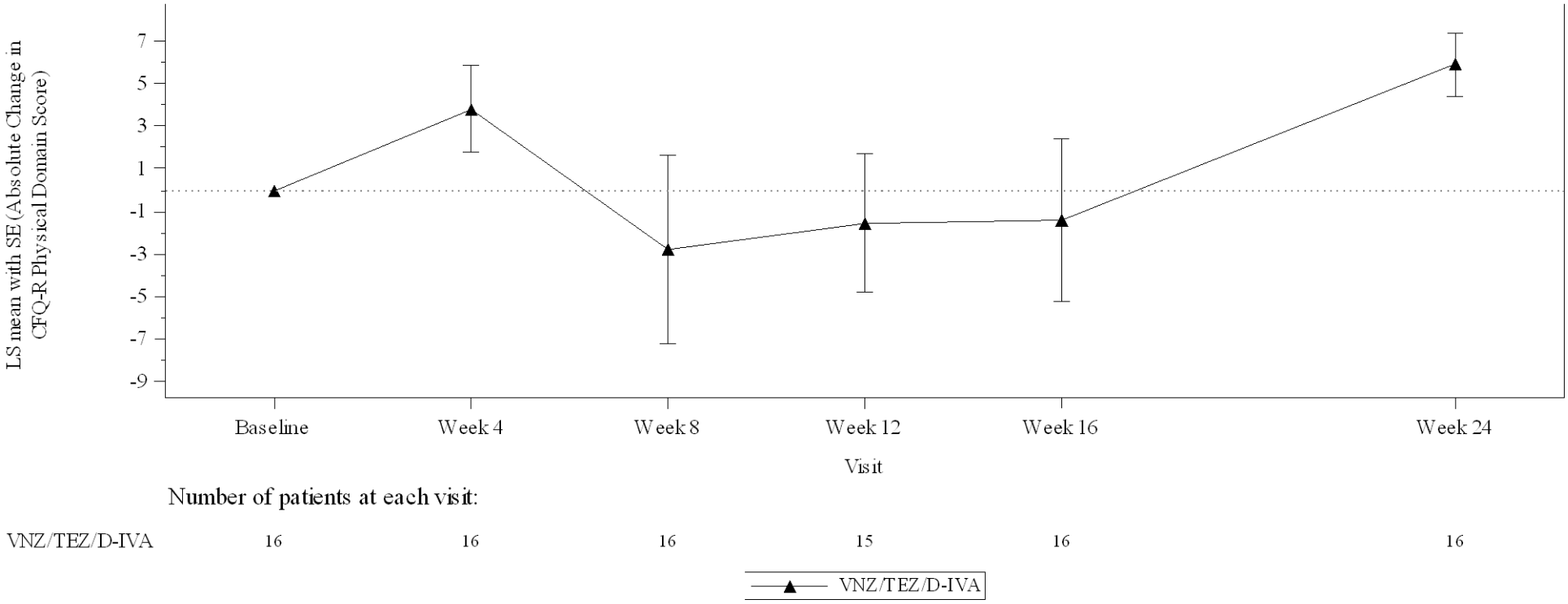
Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical
Region = Rest of World



Number of patients at each visit:

	Baseline	Week 4	Week 8	Week 12	Week 16	Week 24
VNZ/TEZ/D-IVA	16	16	16	15	16	16

VNZ/TEZ/D-IVA

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

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Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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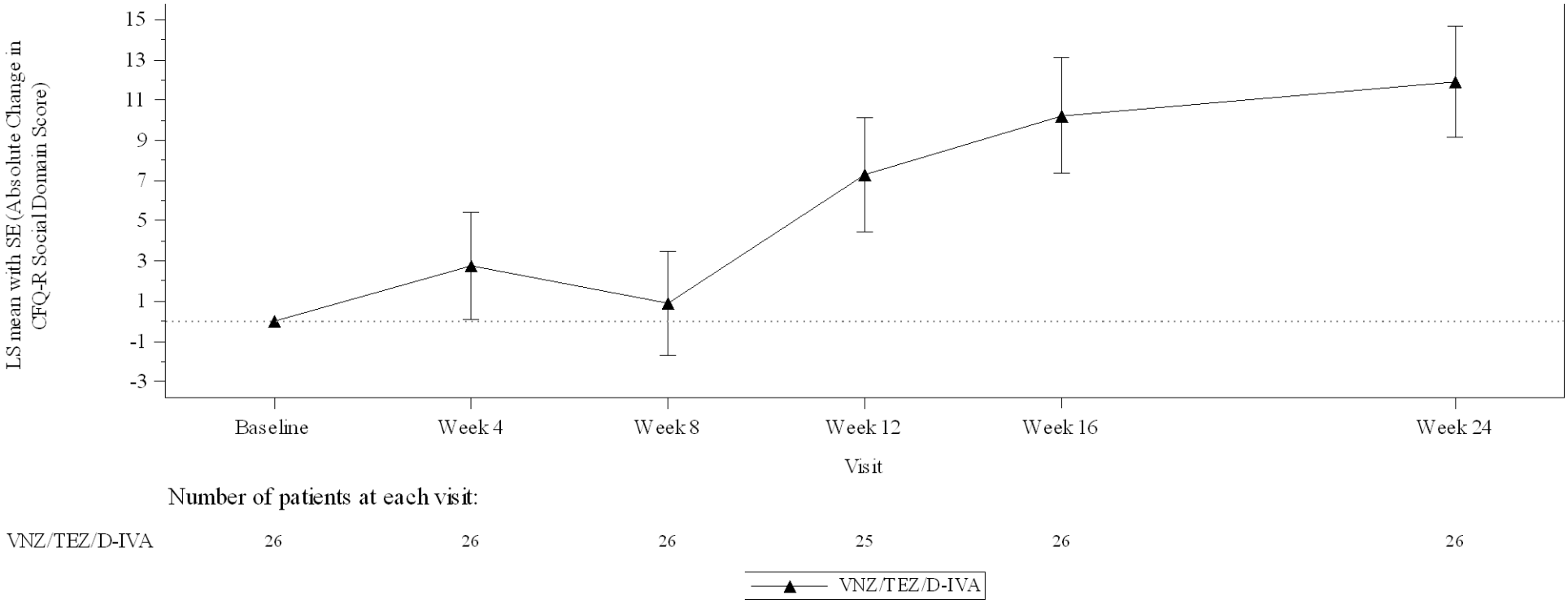
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

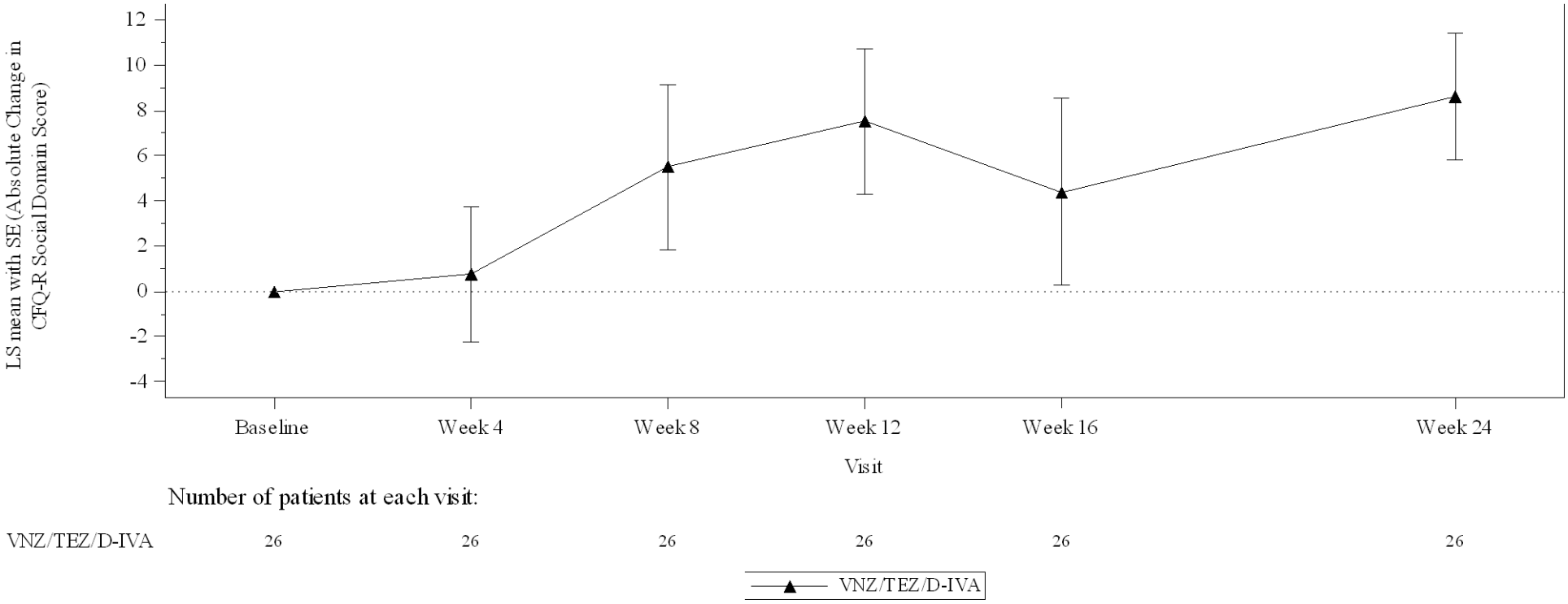
Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Social
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Social
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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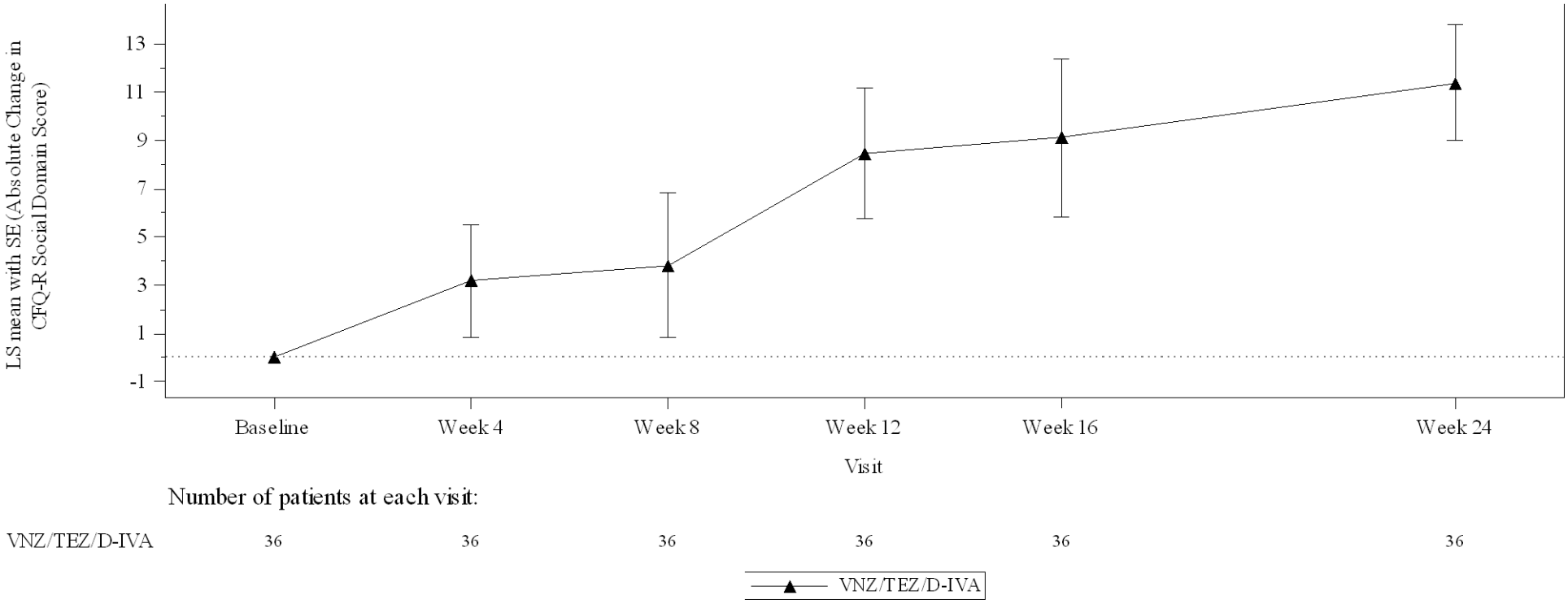
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Social
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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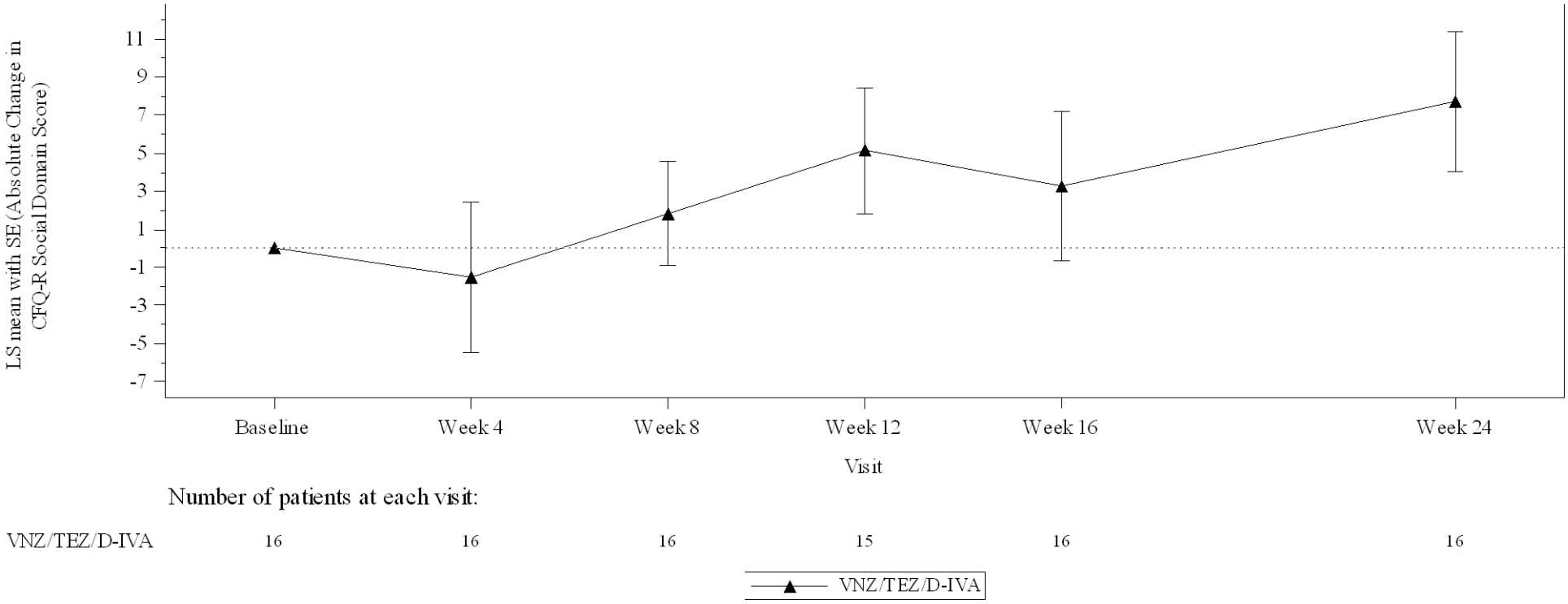
Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Social
Region = Rest of World



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- Baseline is defined as the pre-dose Day 1 value.
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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Social
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Social
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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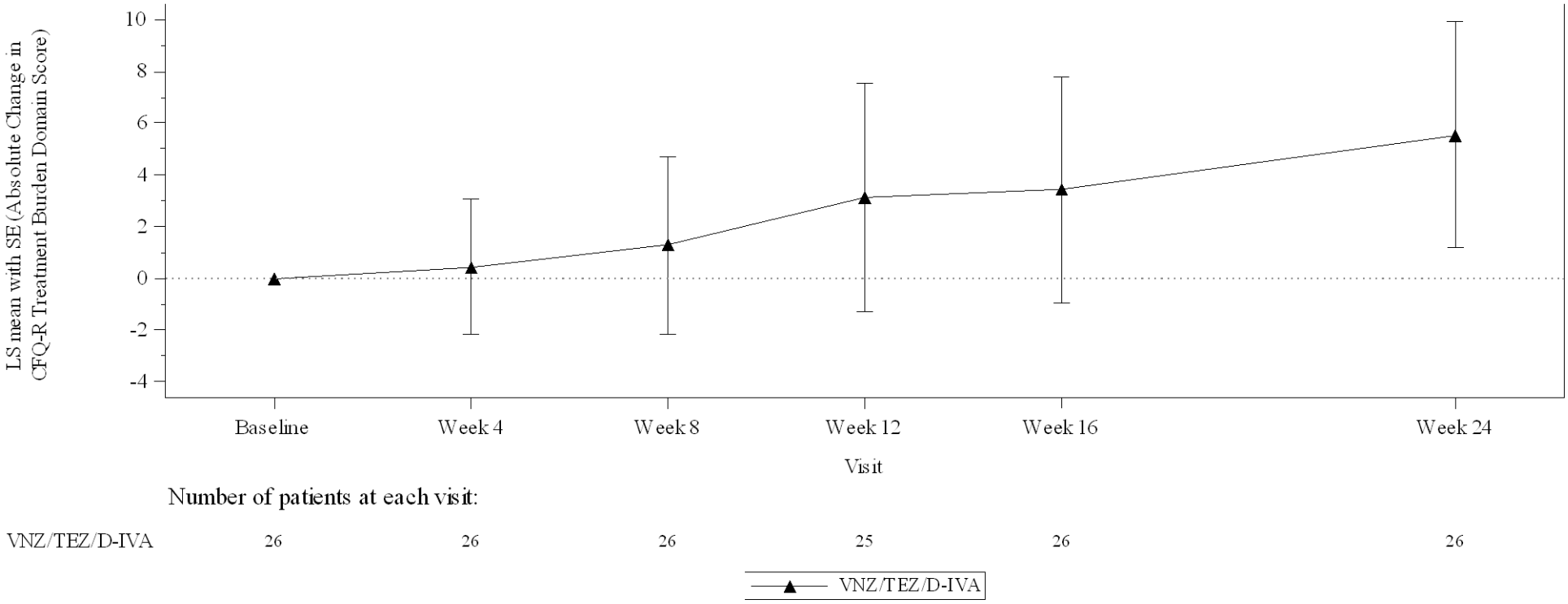
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden
Sex = Male



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- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden
Sex = Female

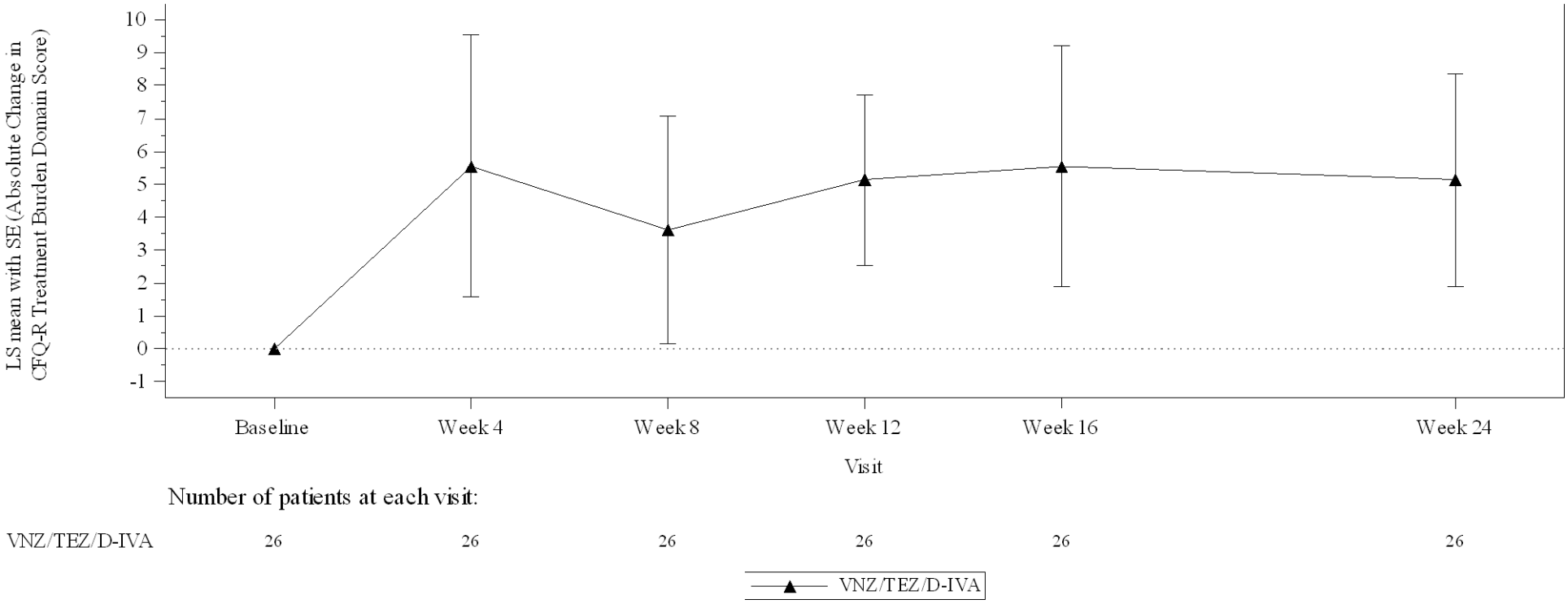

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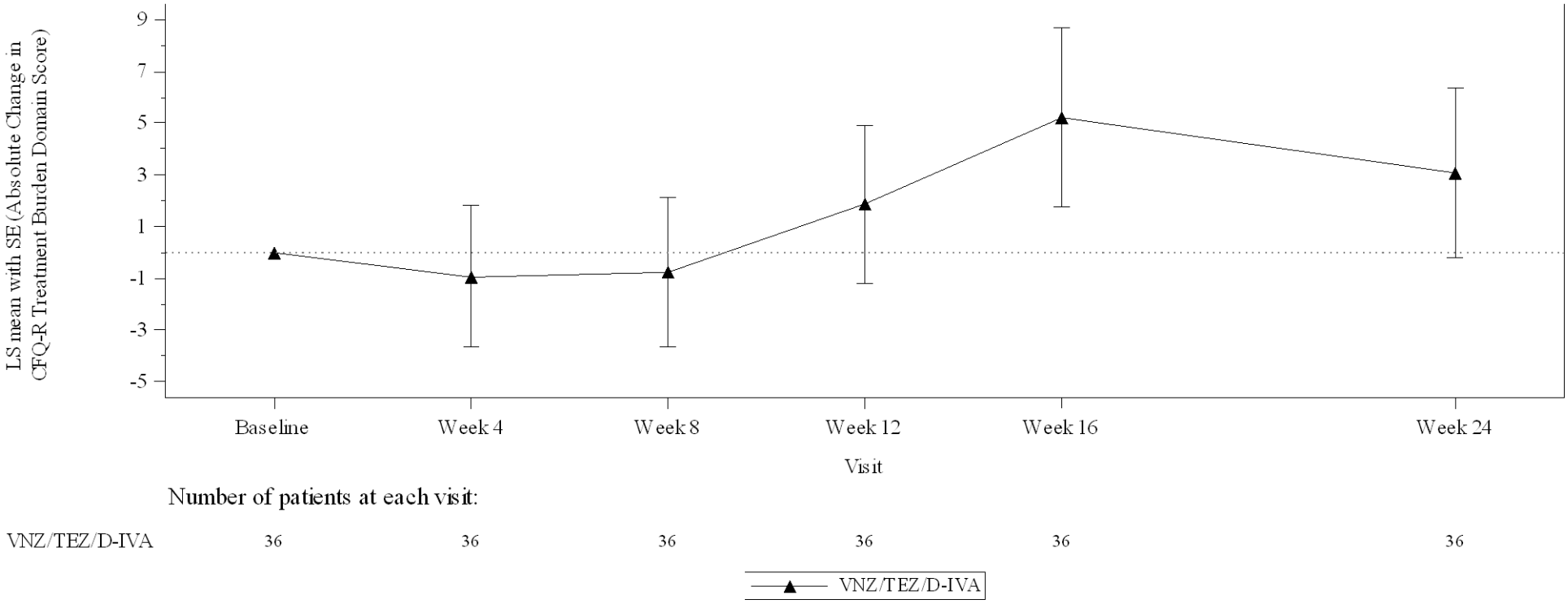
Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden
Region = North America



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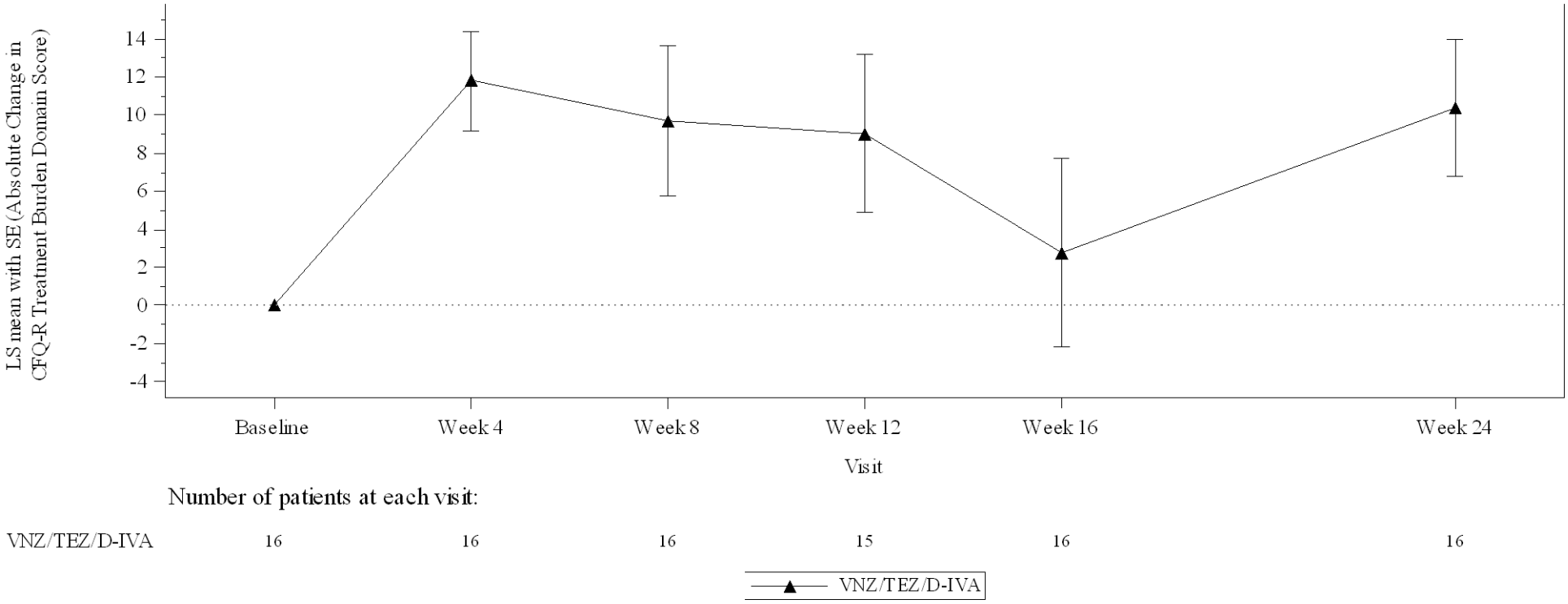
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden
Region = Rest of World



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- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

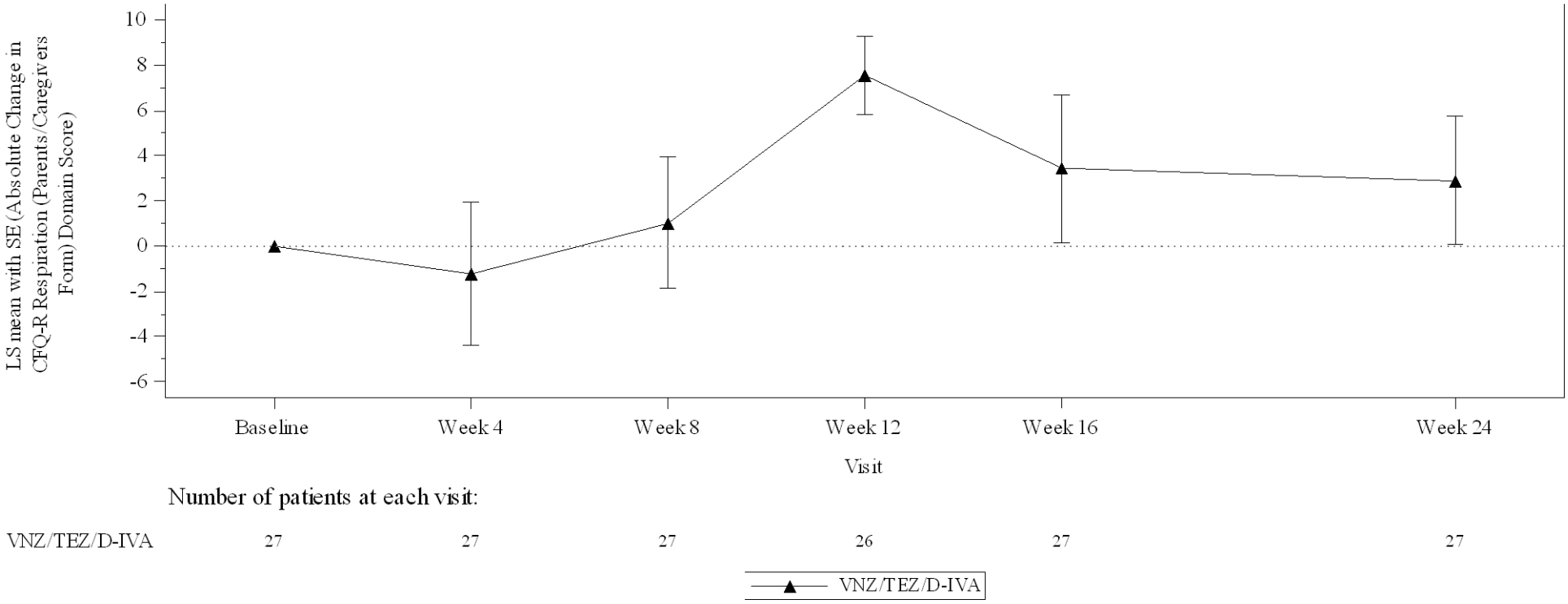
Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:18

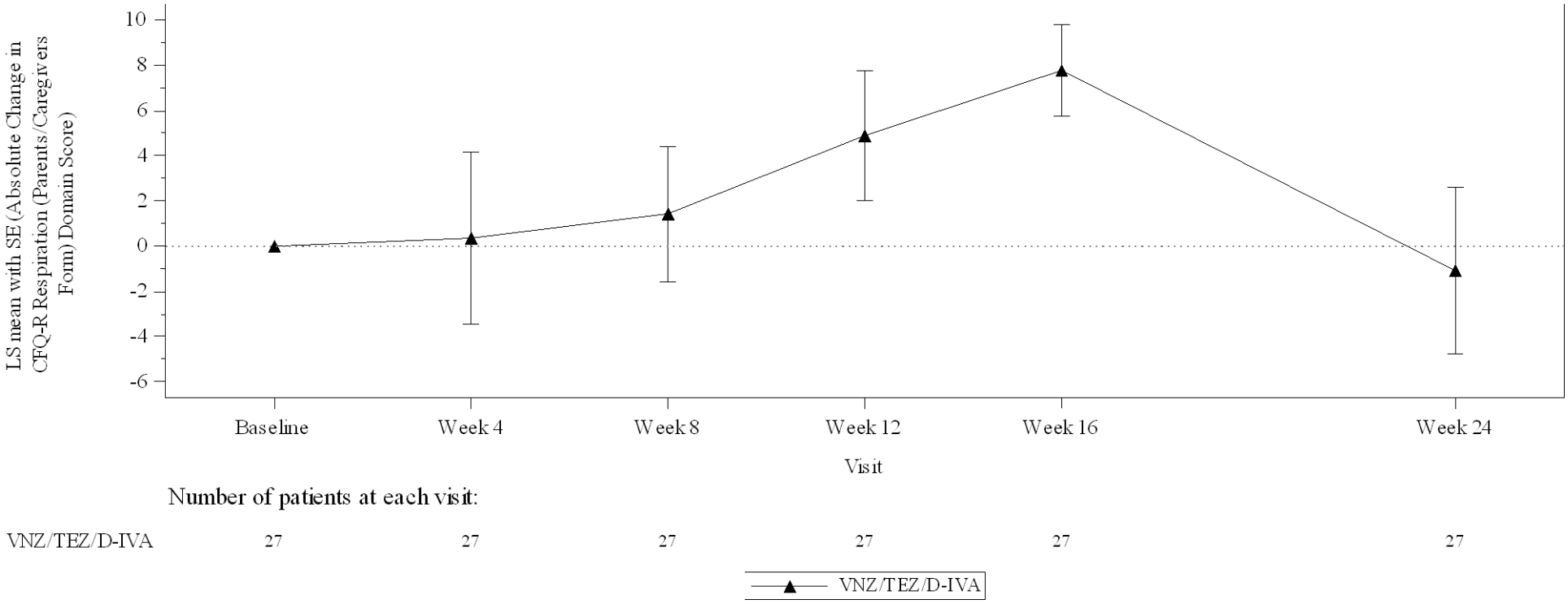
Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

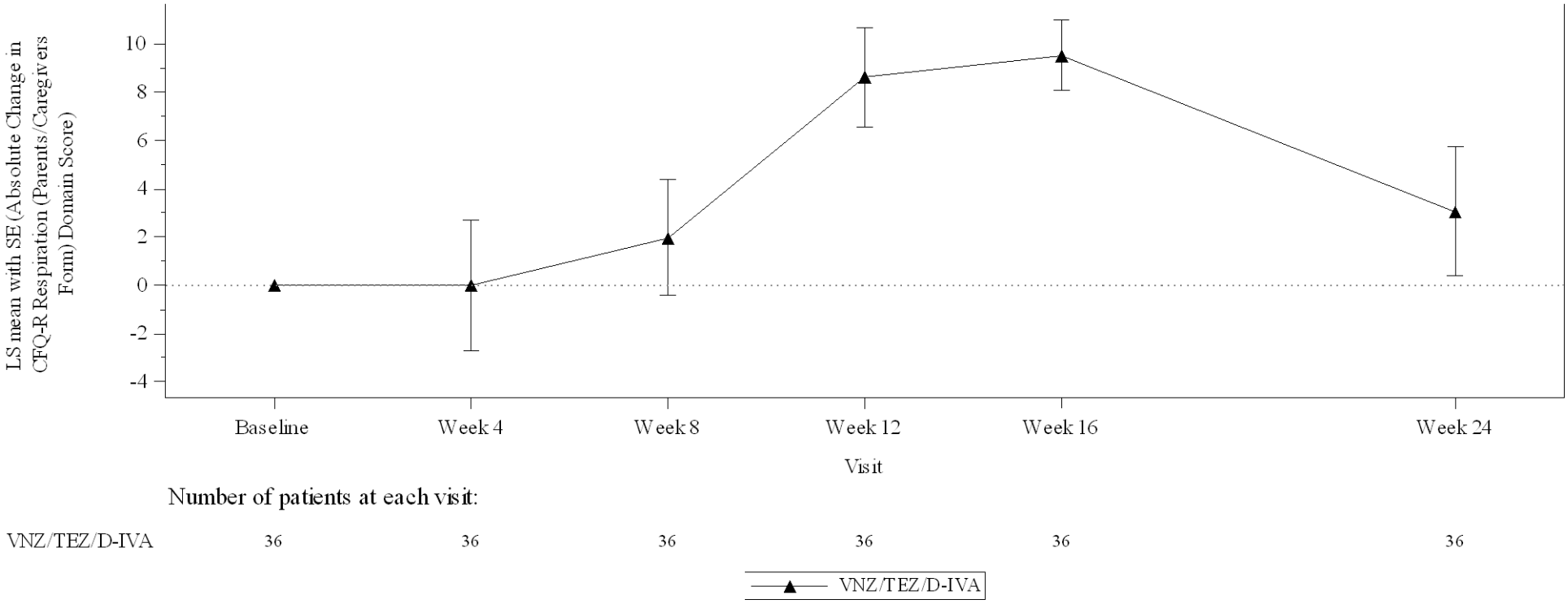
Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

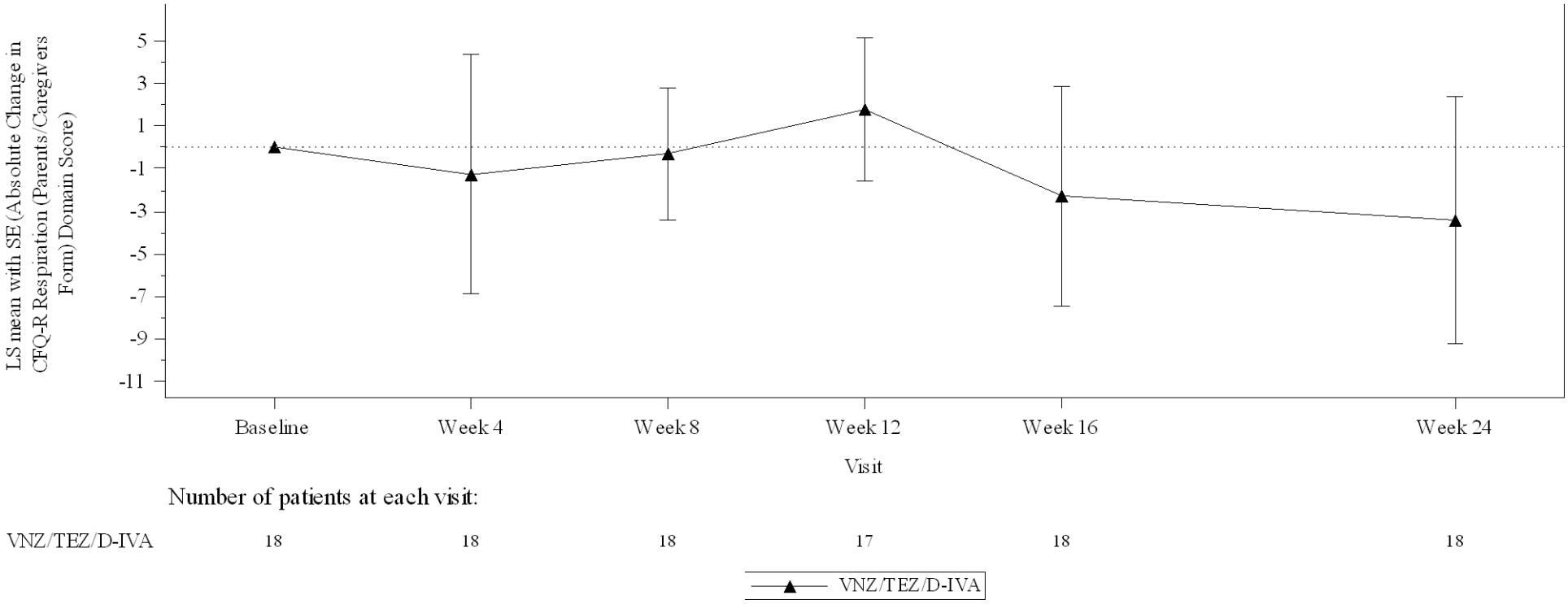
Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

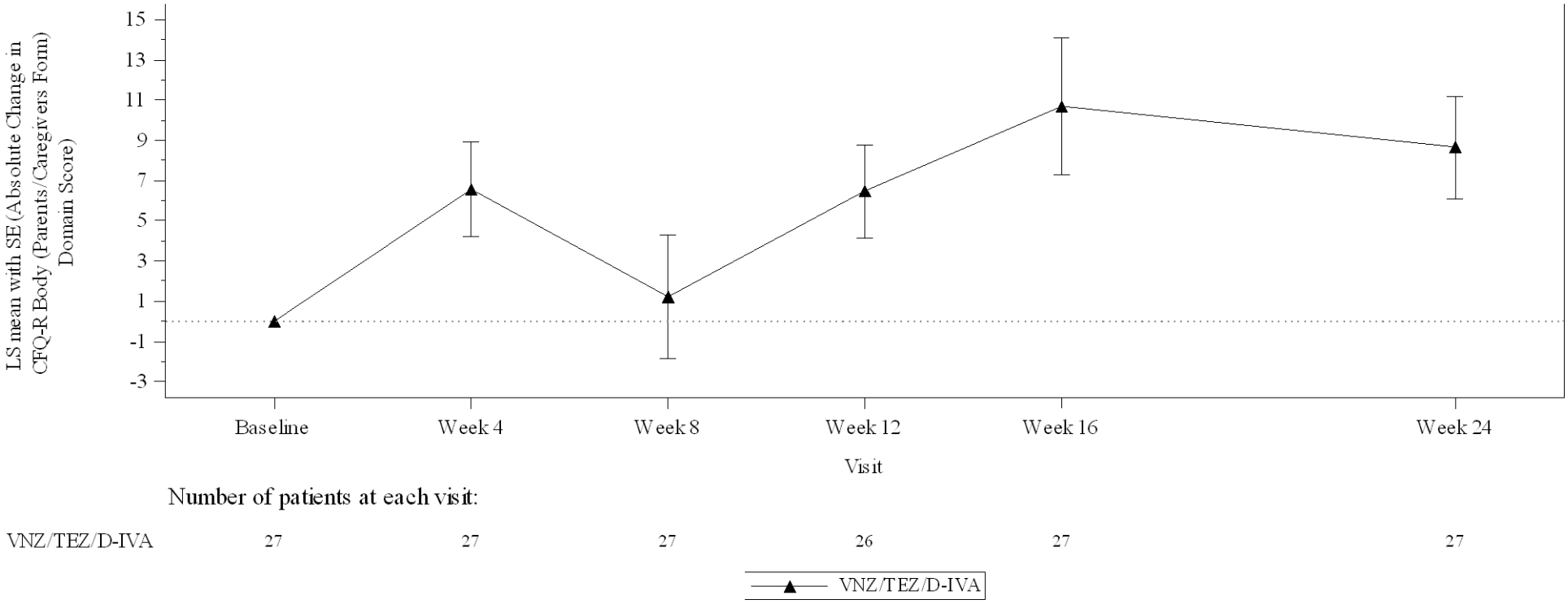
Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

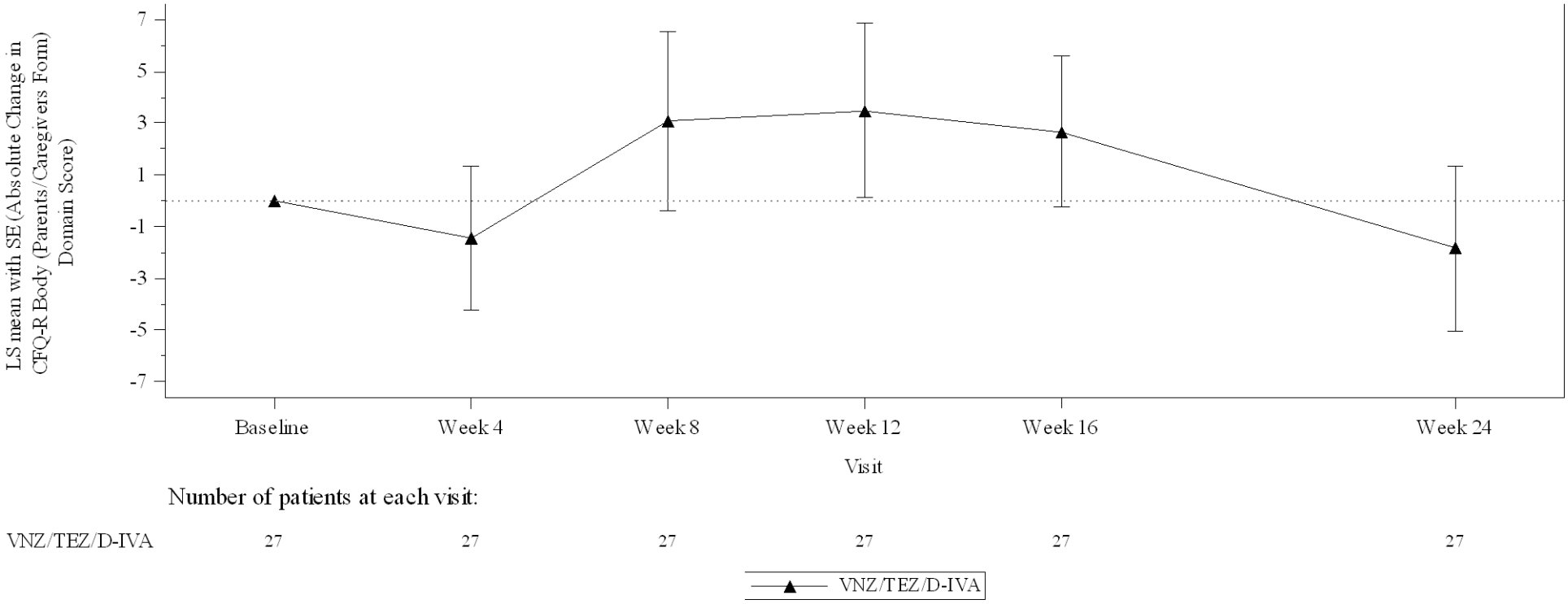
Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

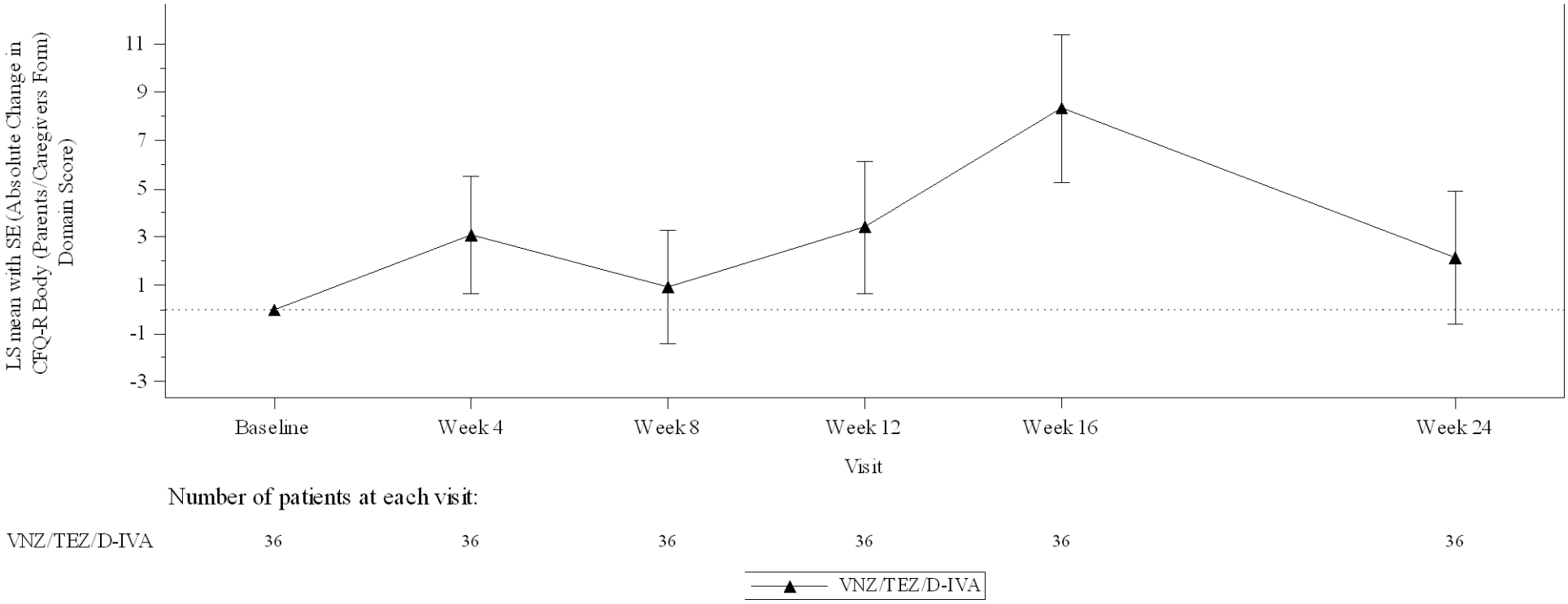
Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

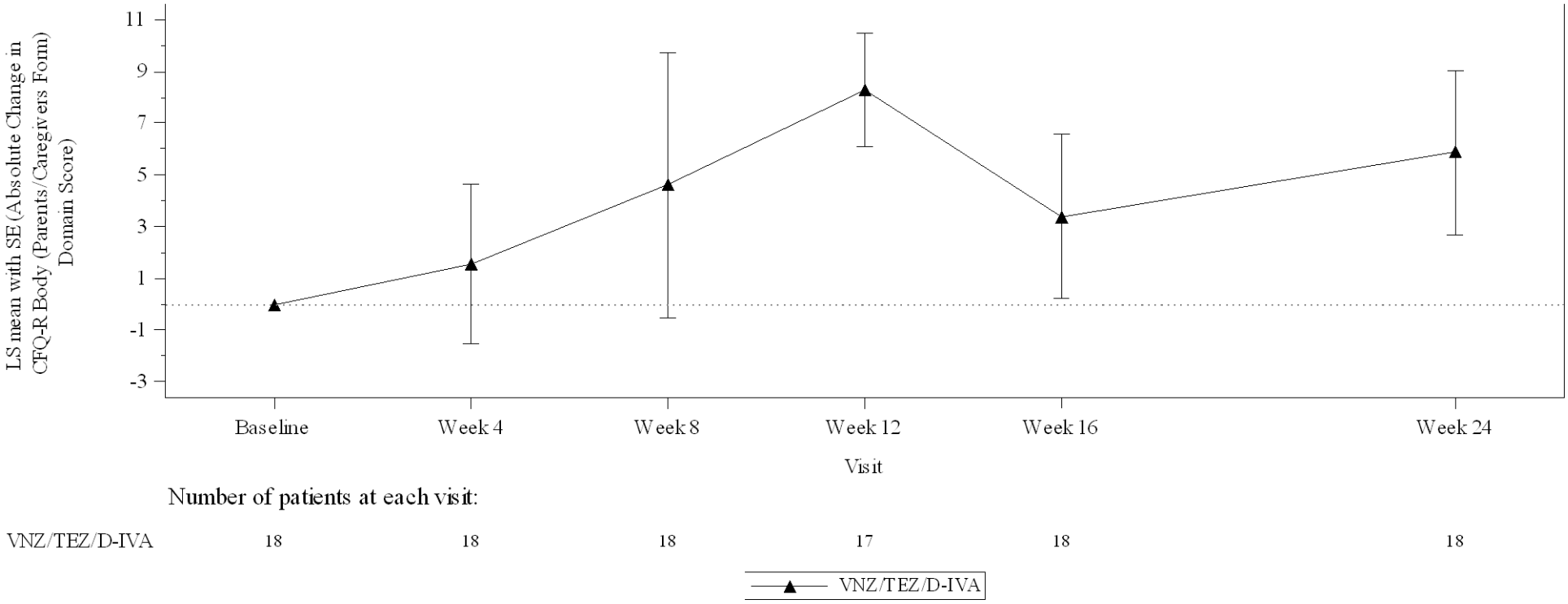
Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

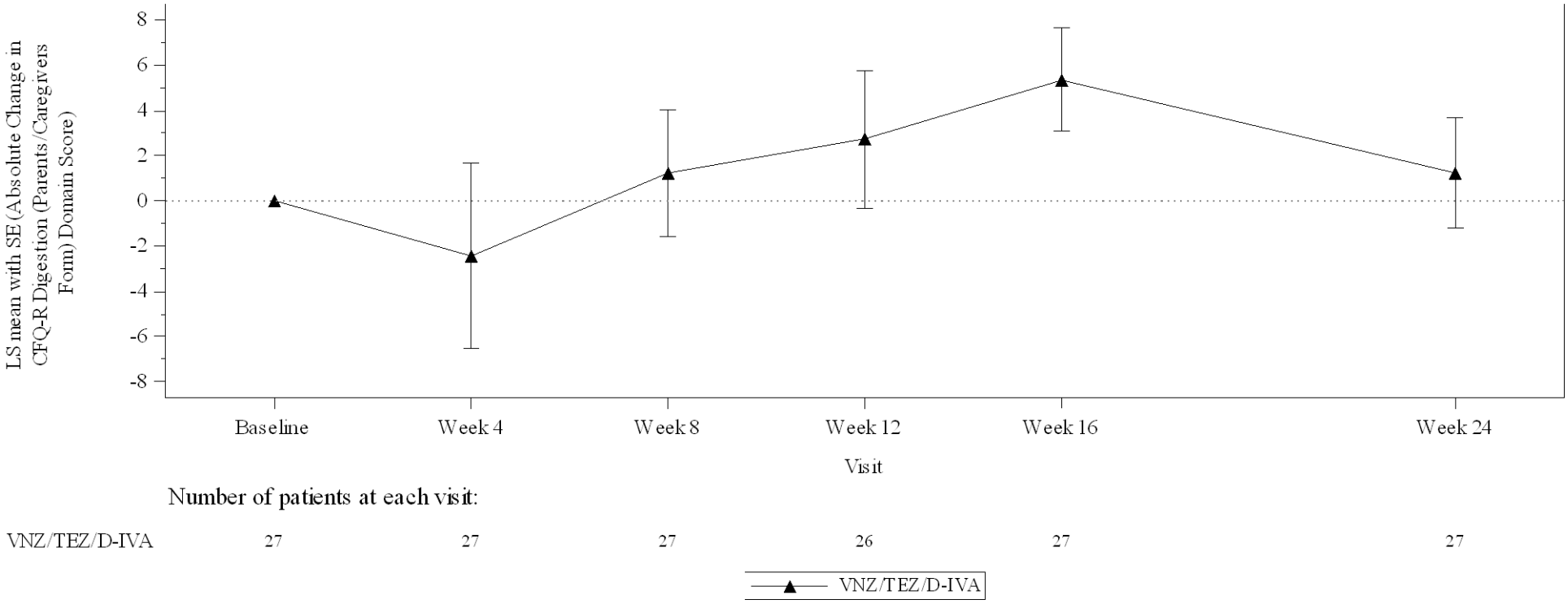
Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

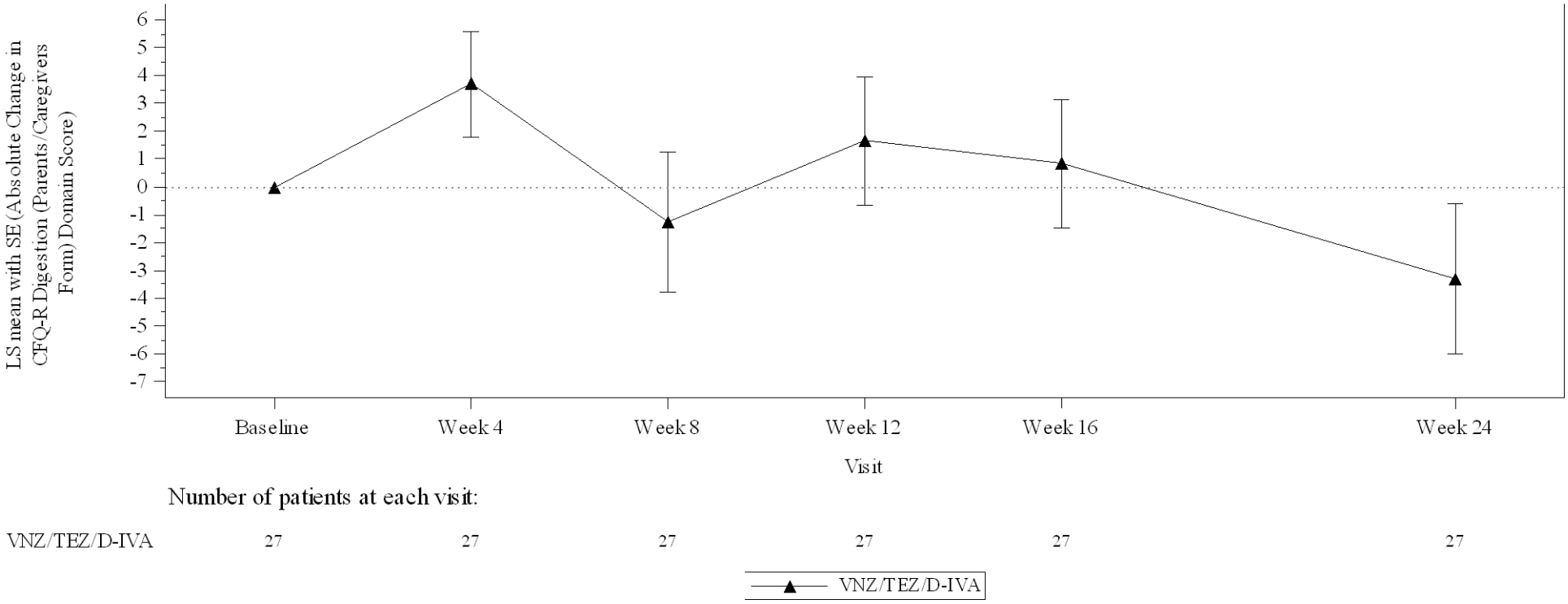
Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

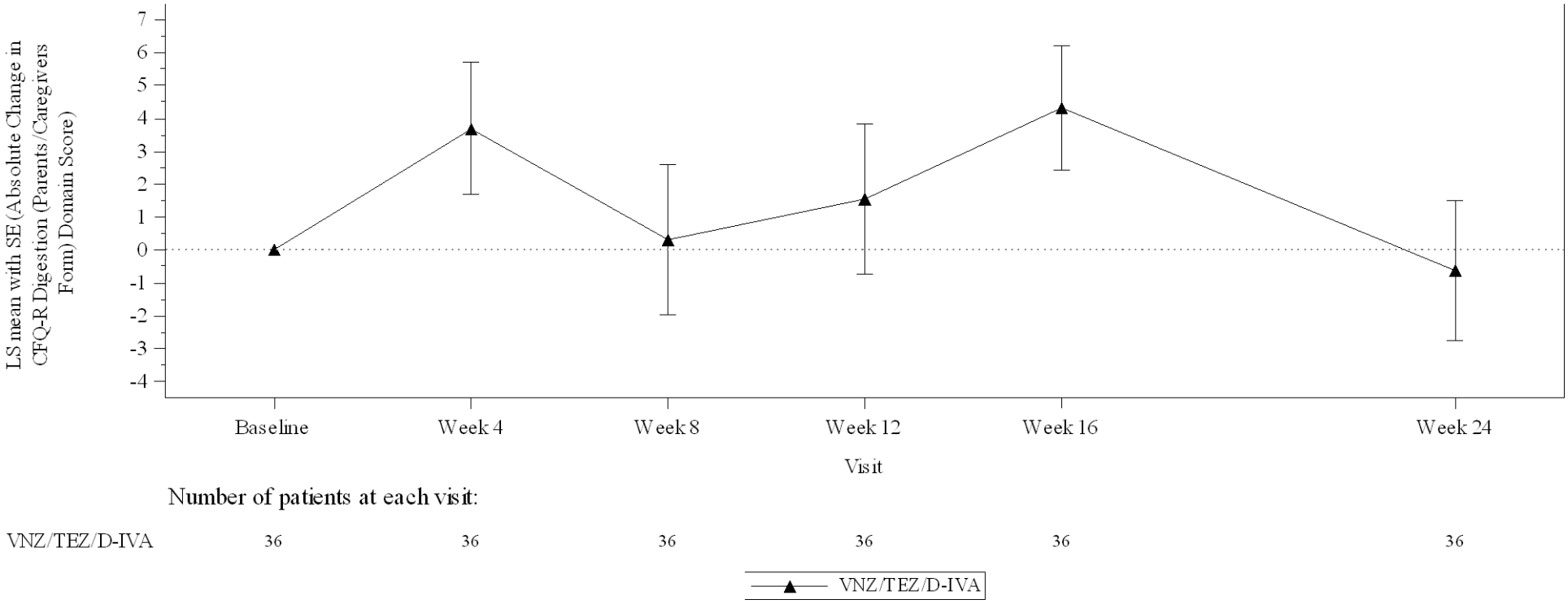
Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

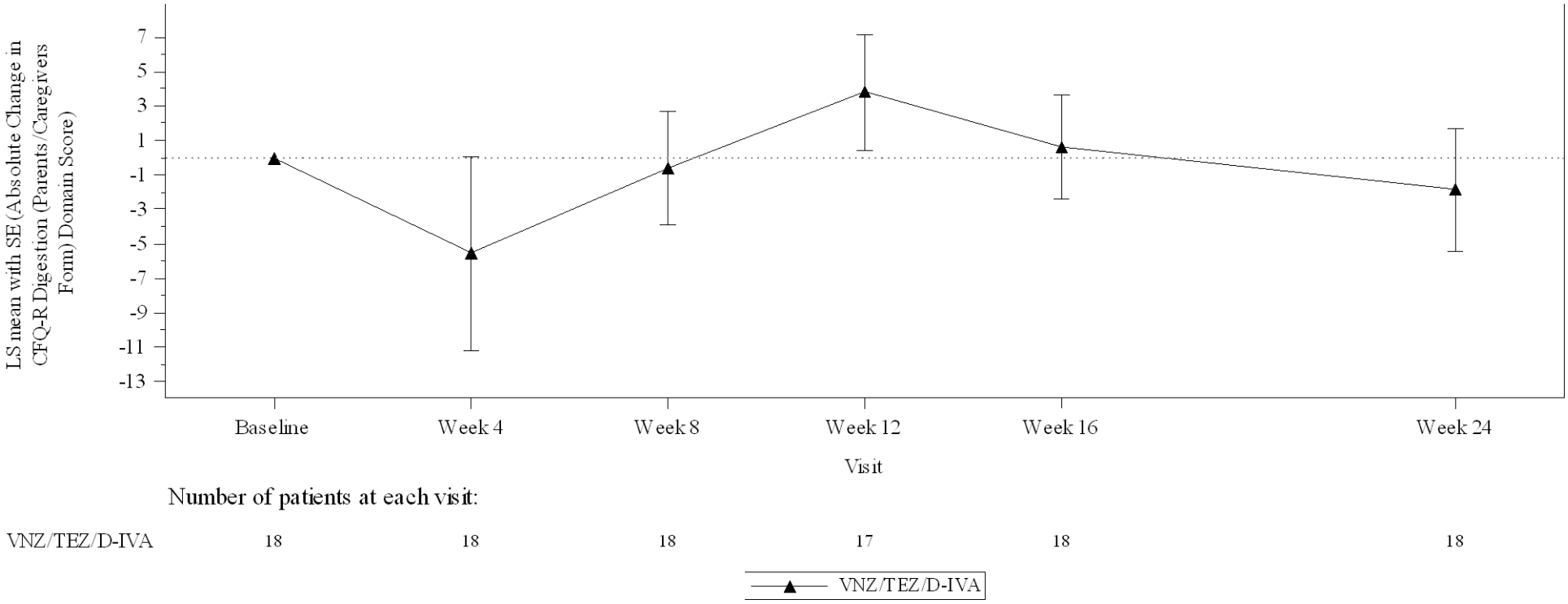
Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World



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- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

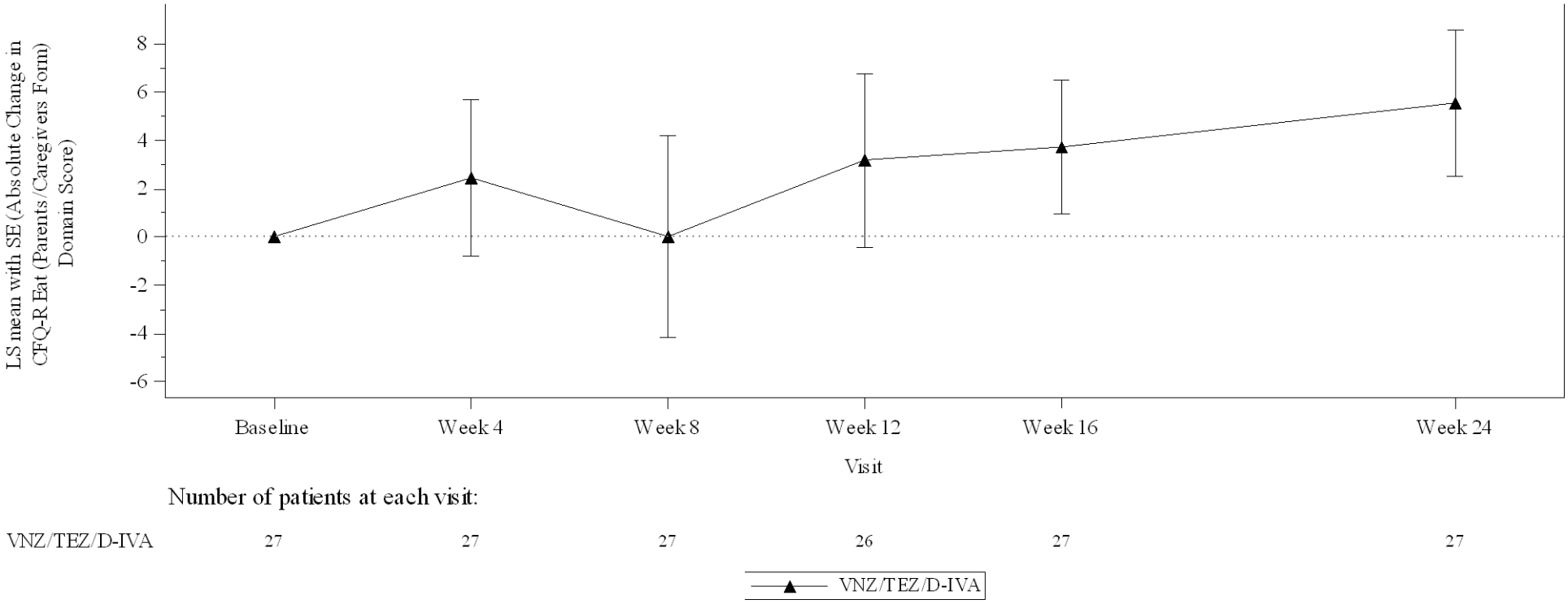
Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

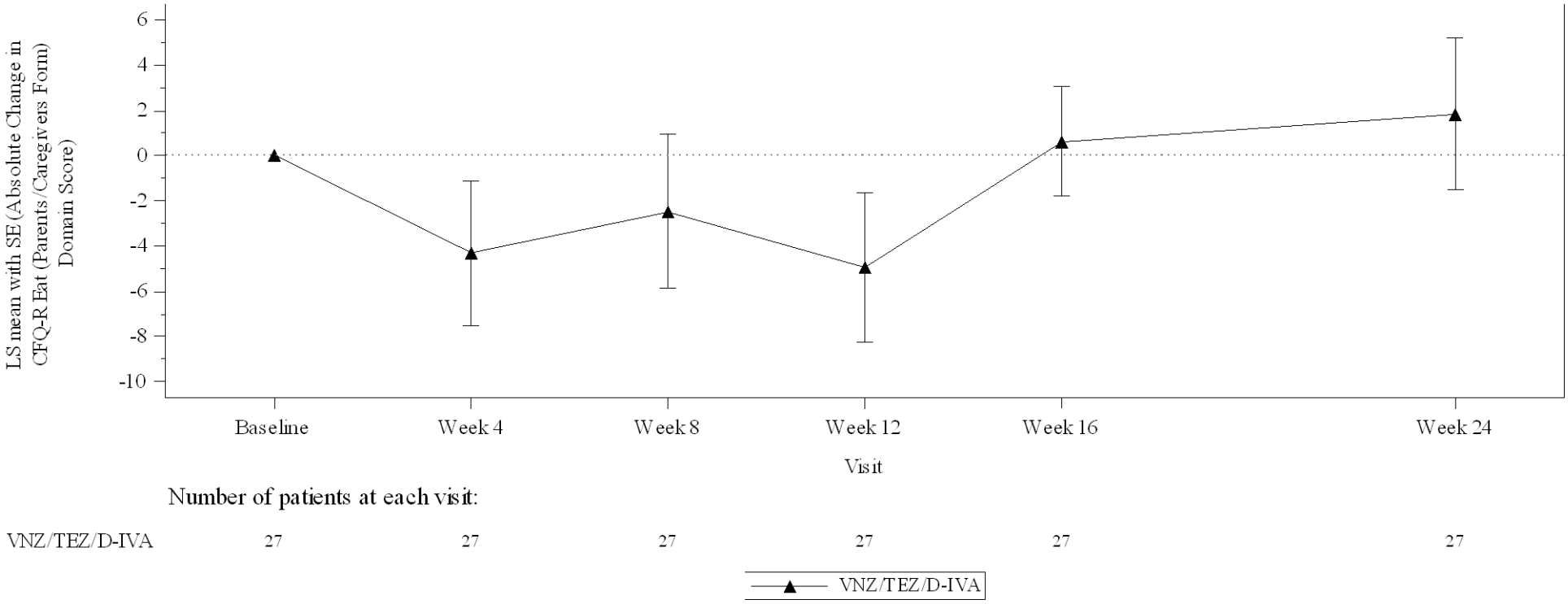
Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Sex = Female



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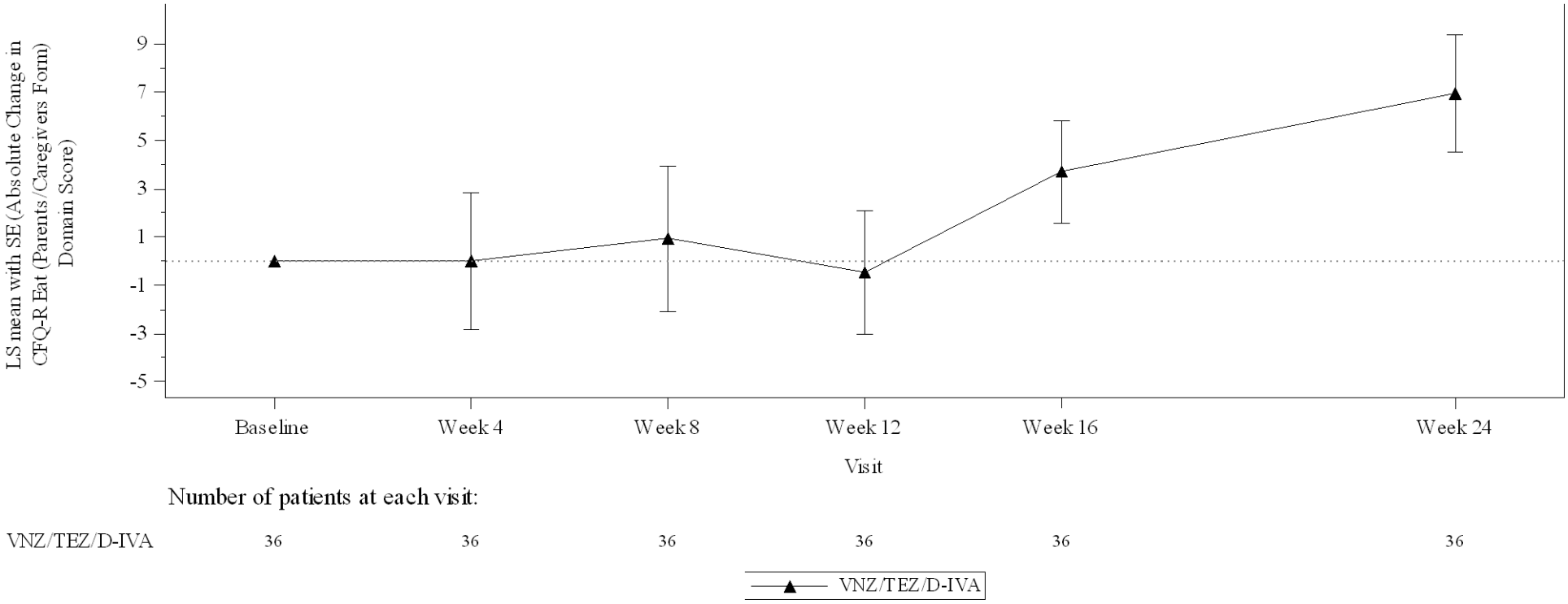
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

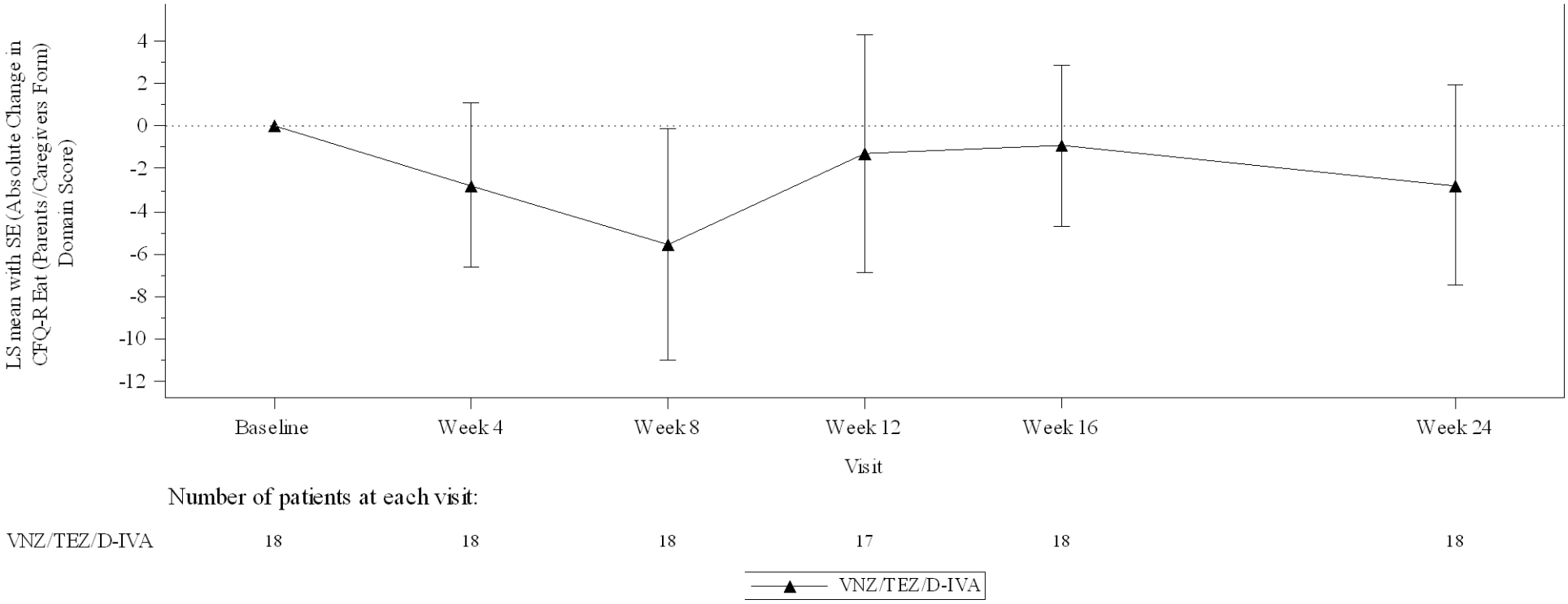


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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Sex = Male

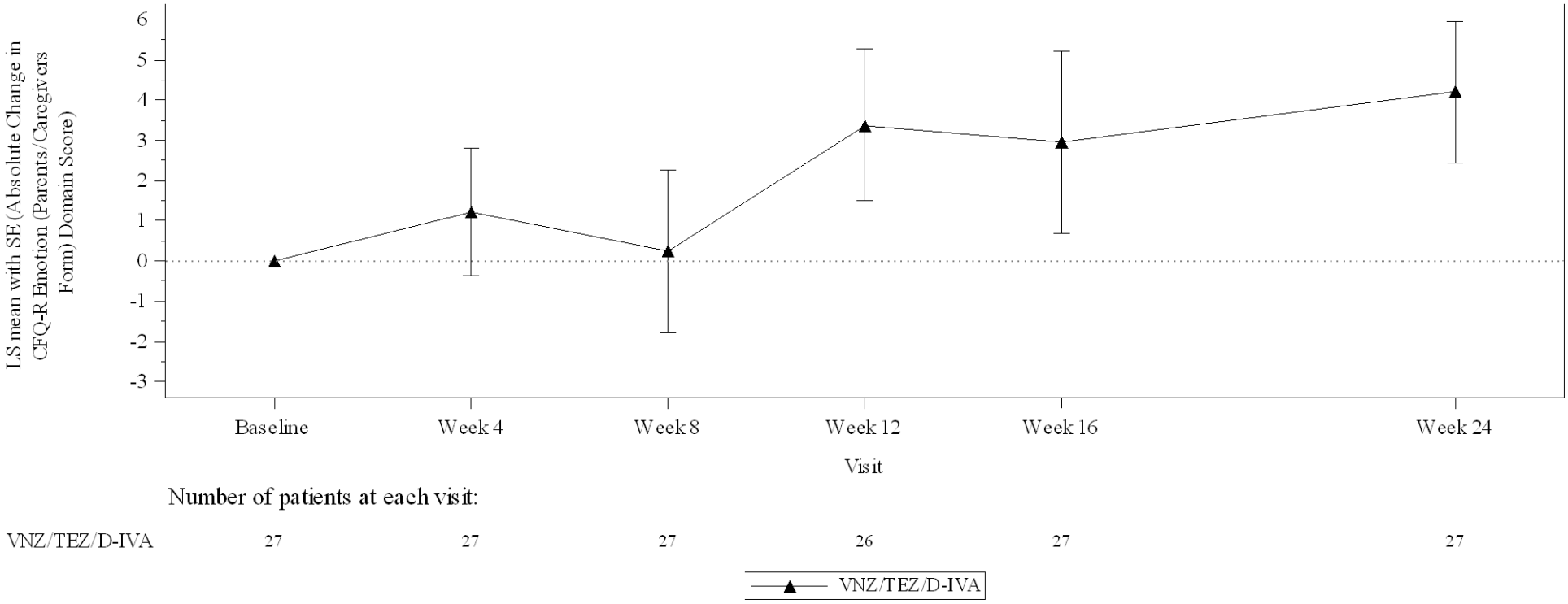

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Sex = Female

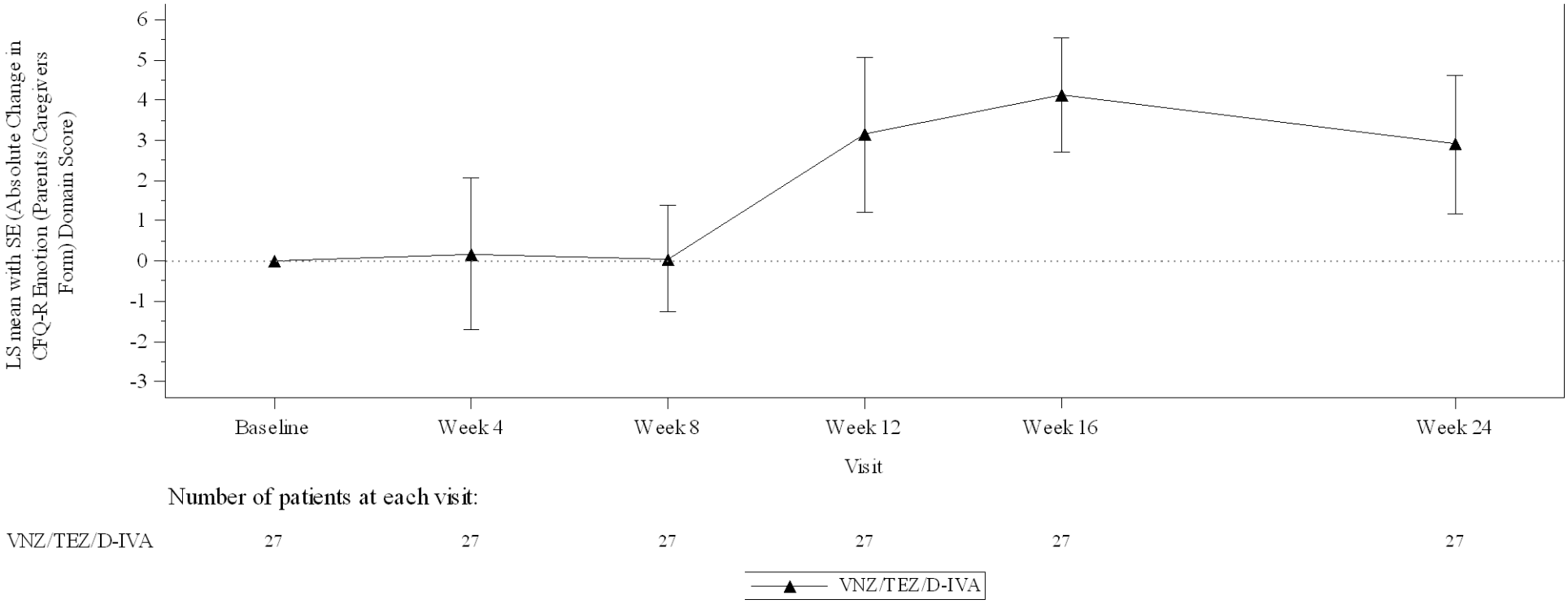

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Region = North America

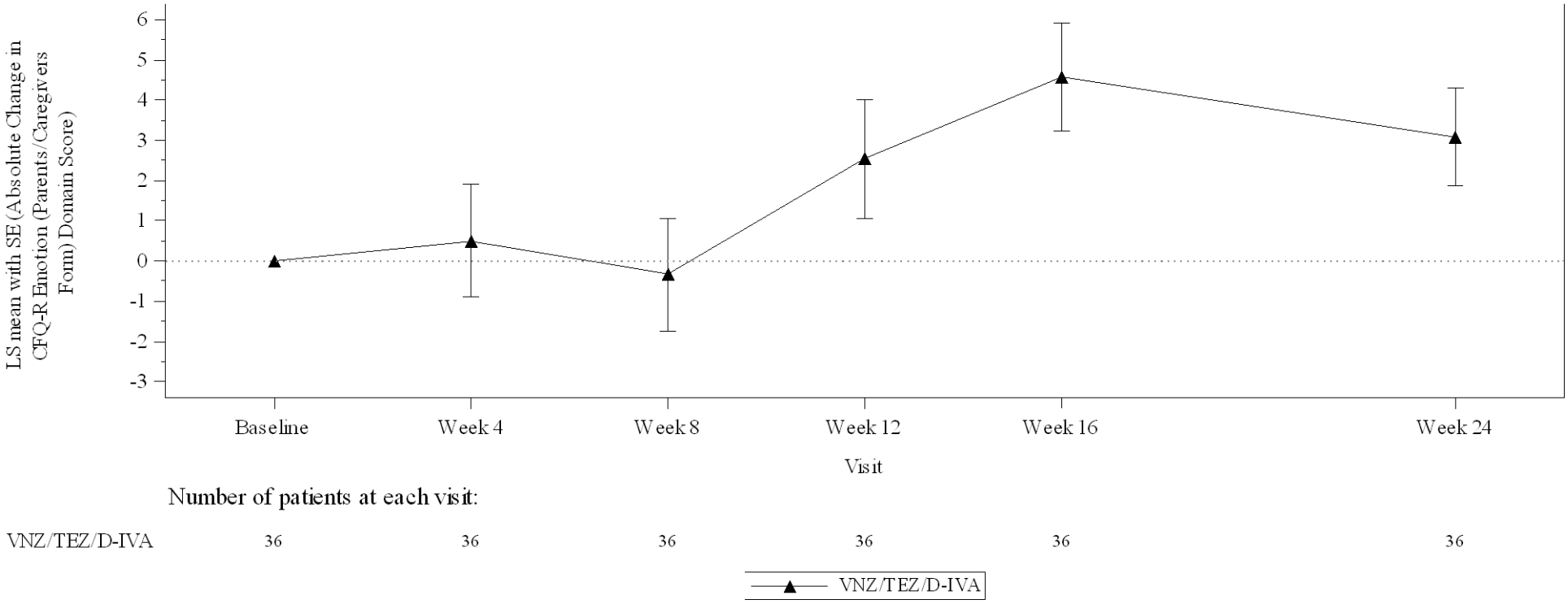

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

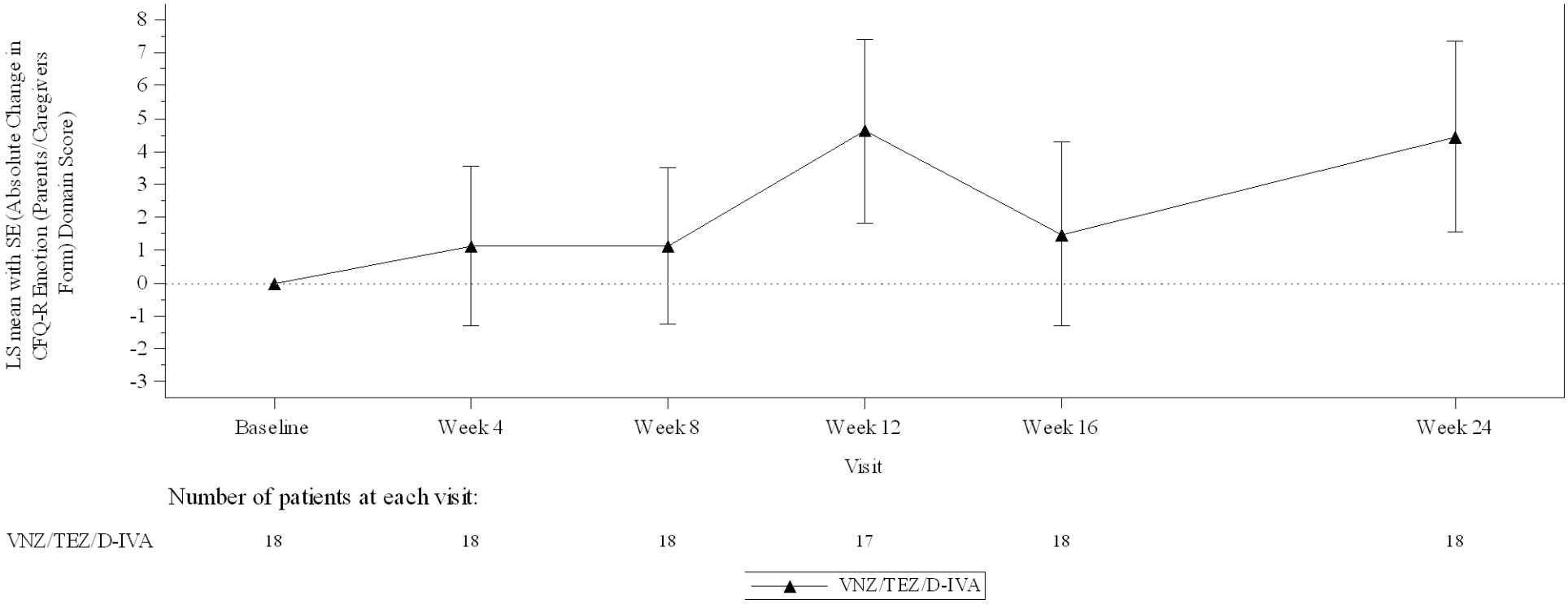

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

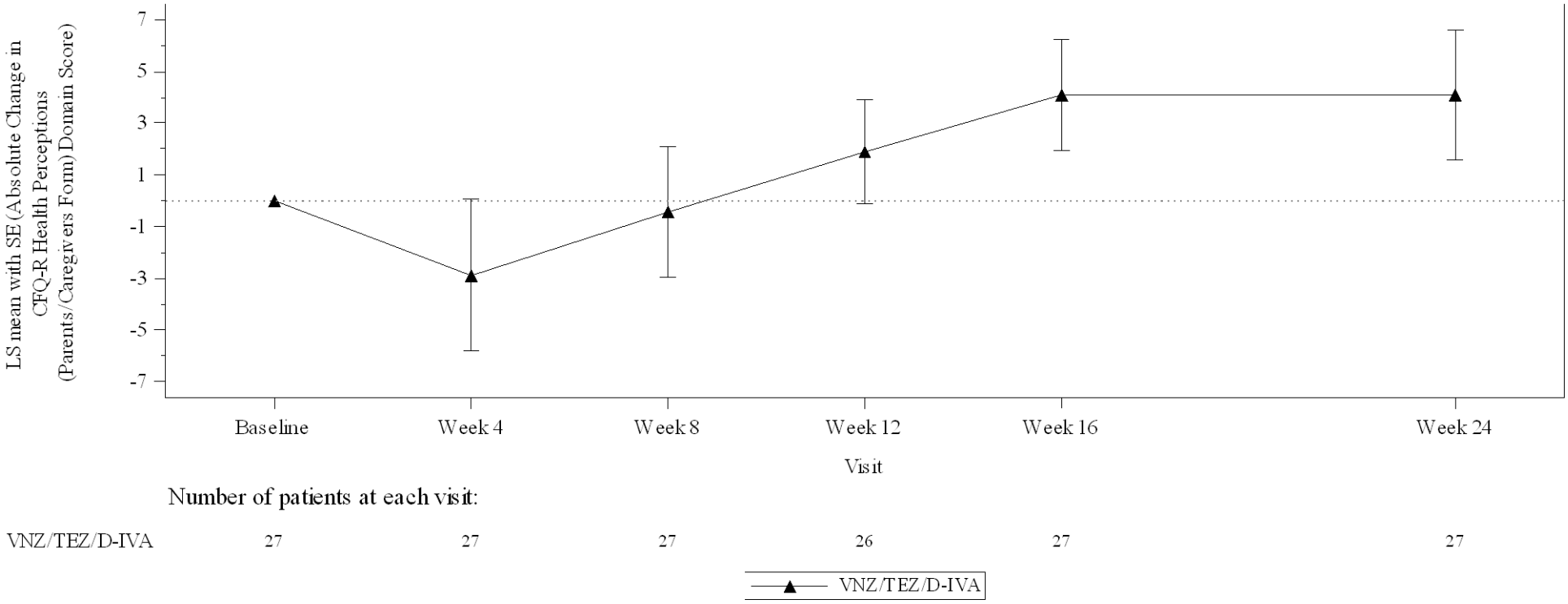

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

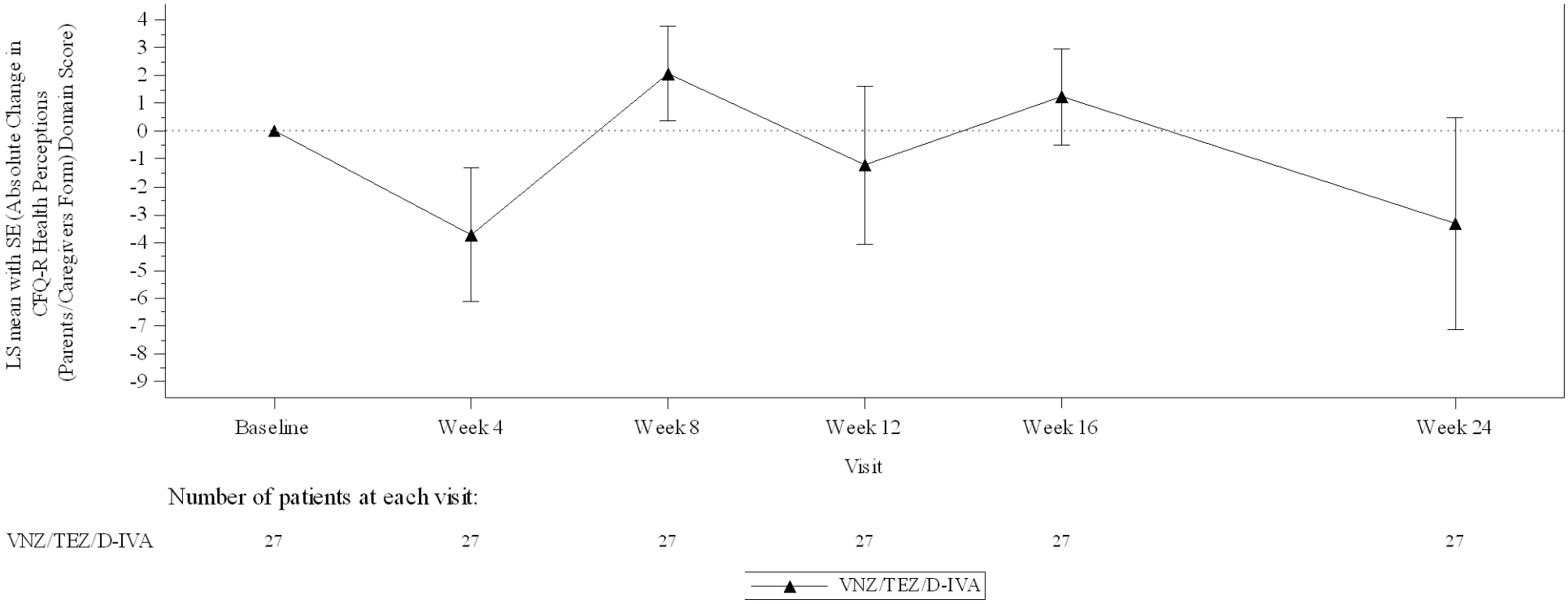

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Figure 2.2.2.10.6
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non-(F/MF)
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

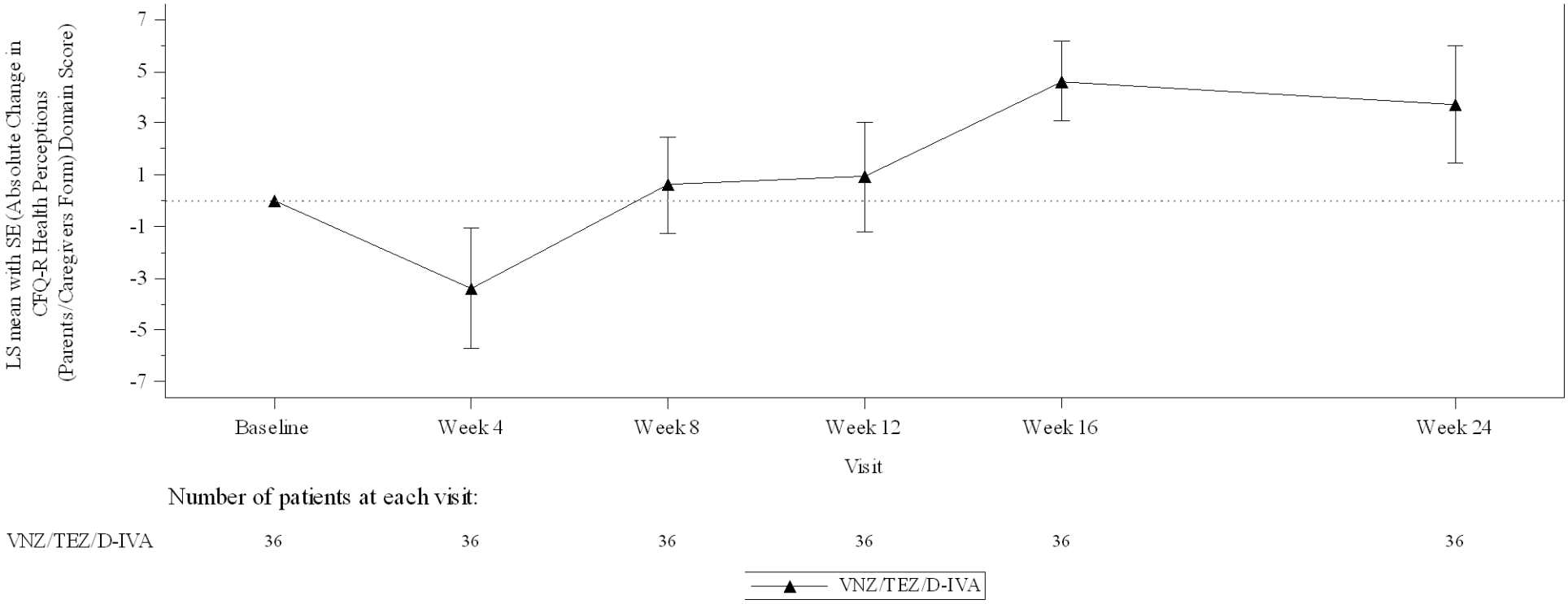

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

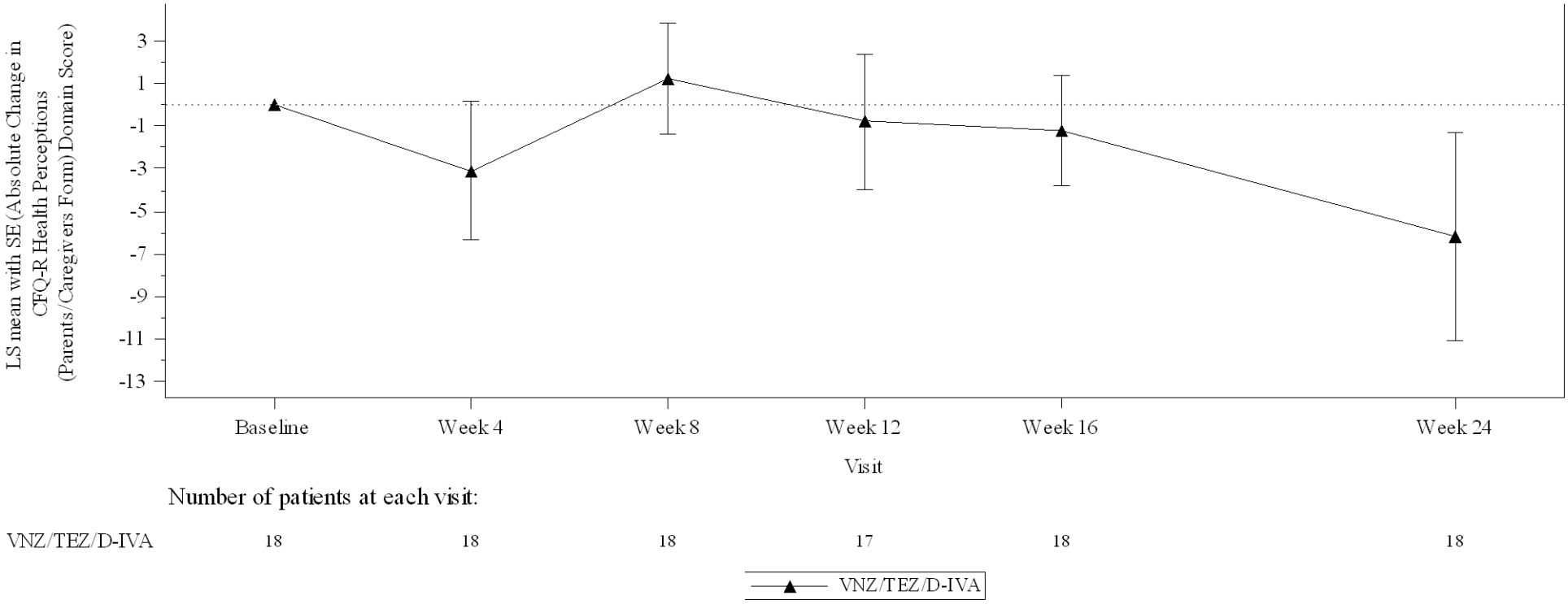

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Sex = Male

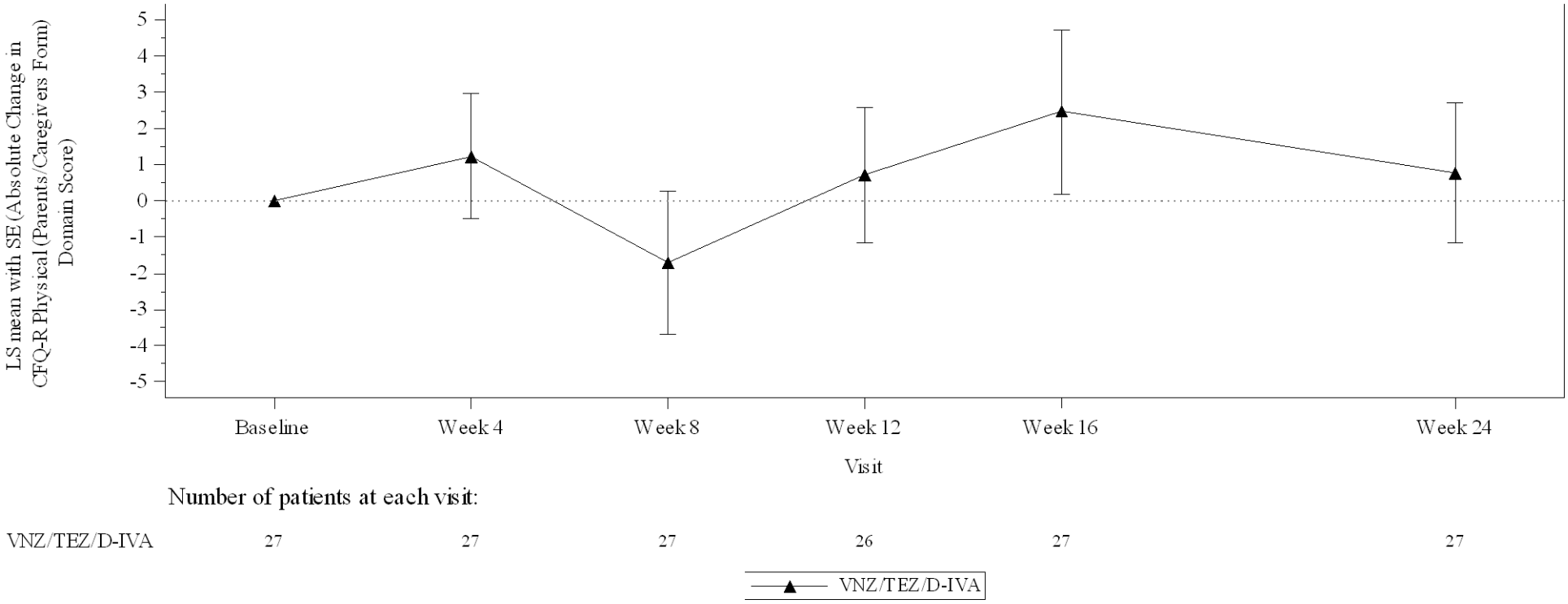

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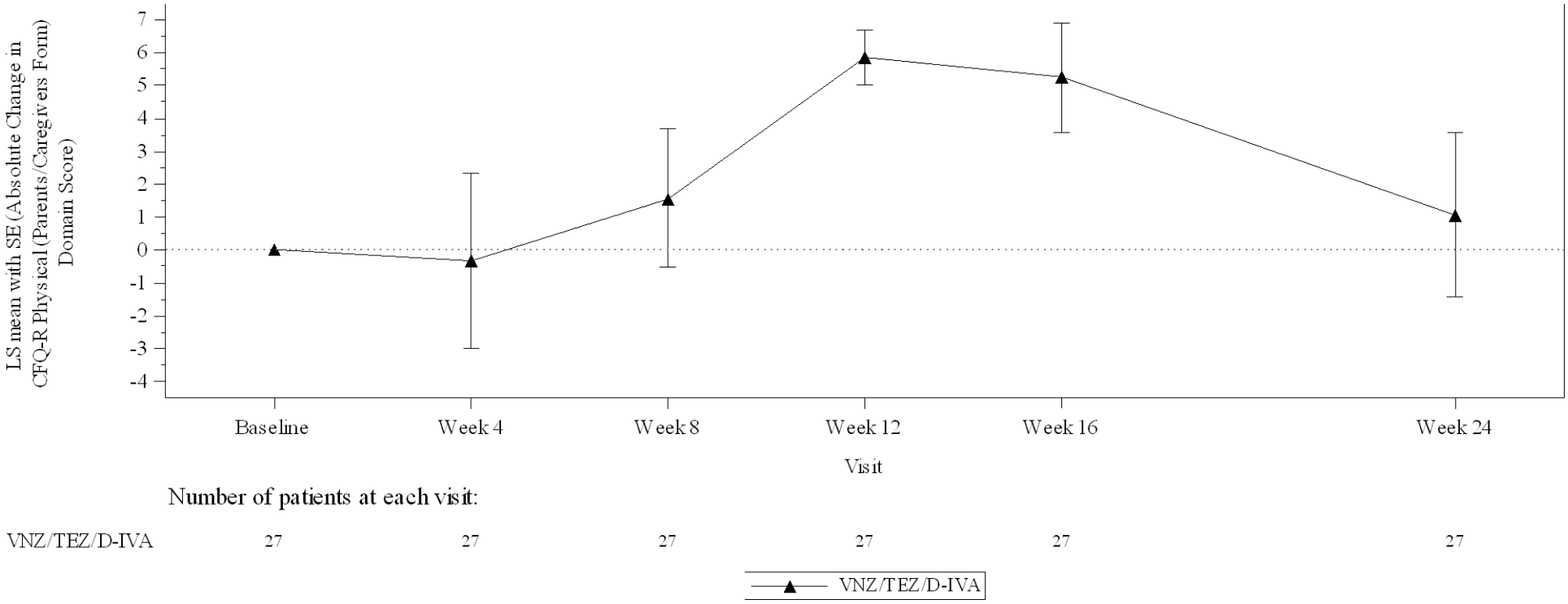
Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Sex = Female



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non-(F/MF)
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Region = North America

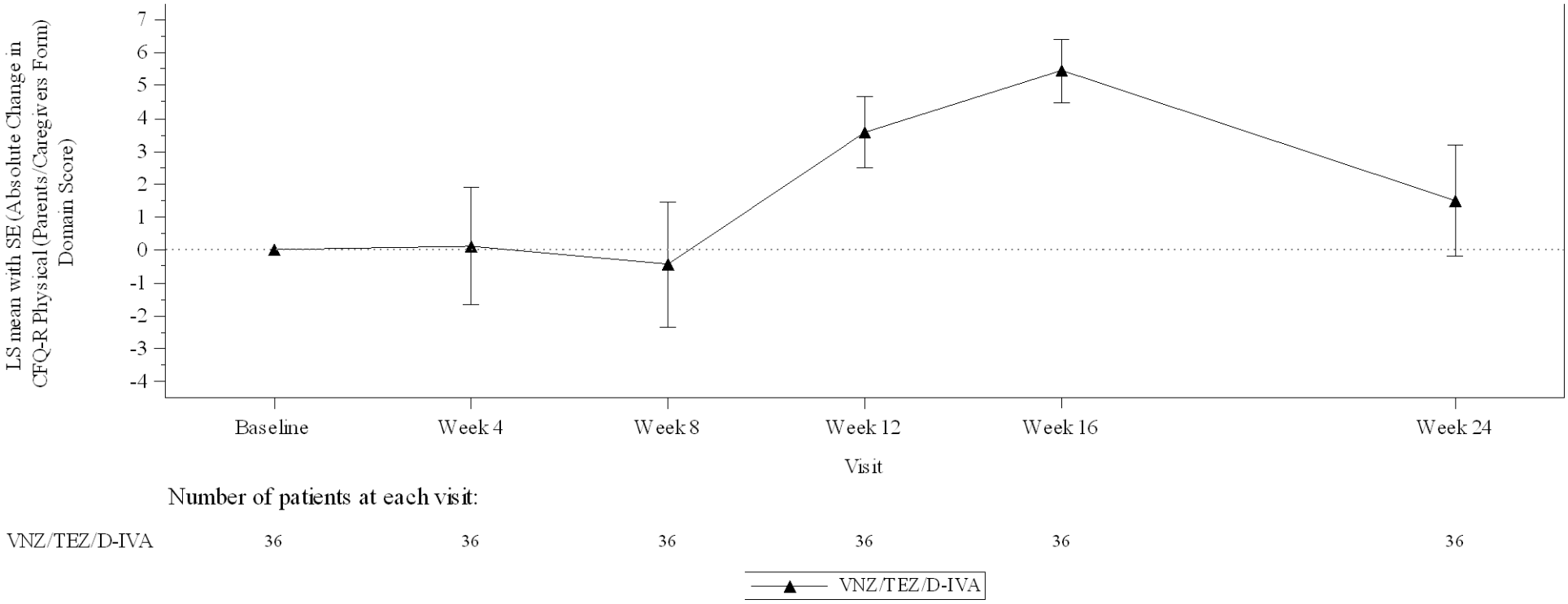

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Figure 2.2.2.10.6
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non-(F/MF)
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

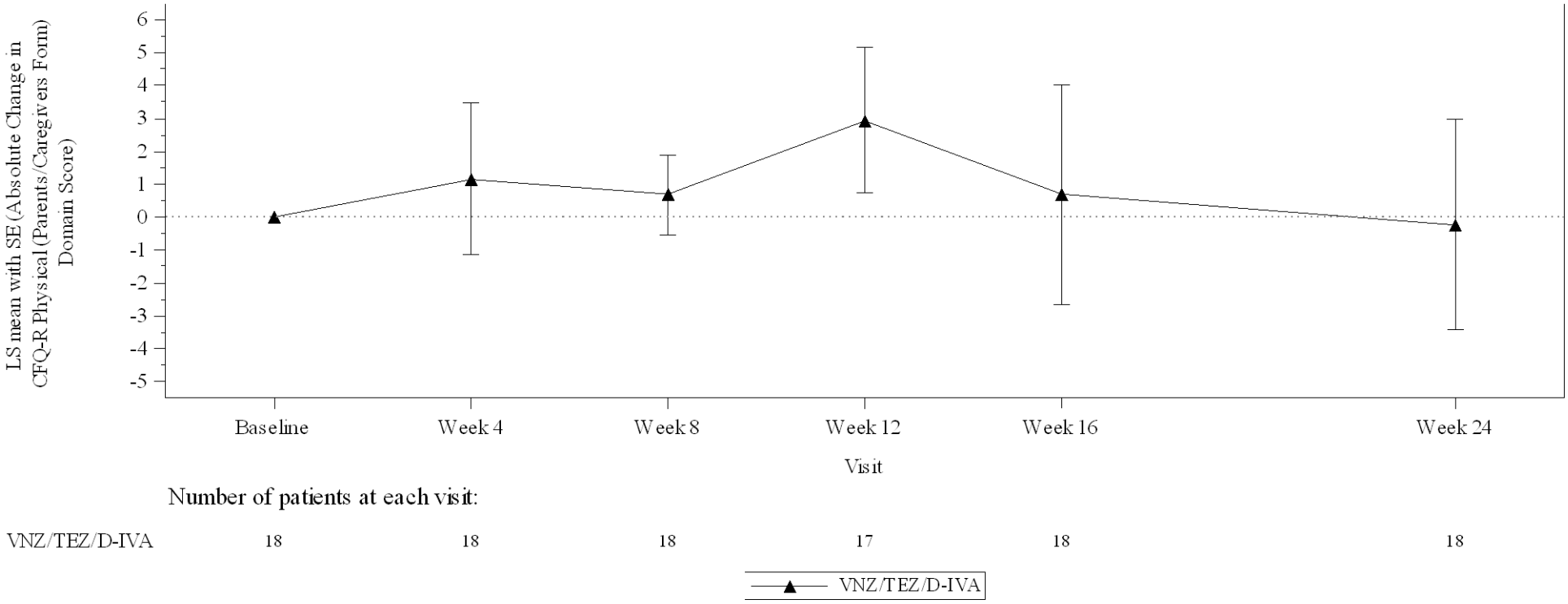

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.10.6
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non-(F/MF)
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

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- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Sex = Male

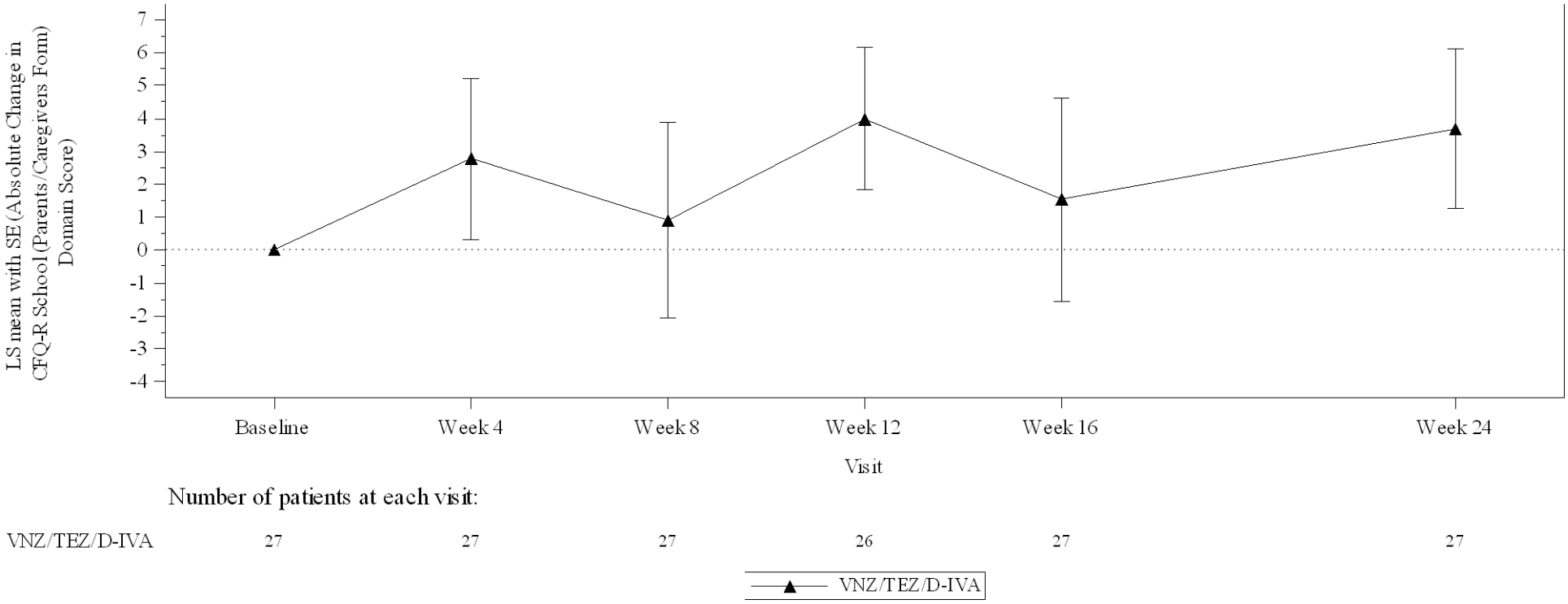

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Sex = Female

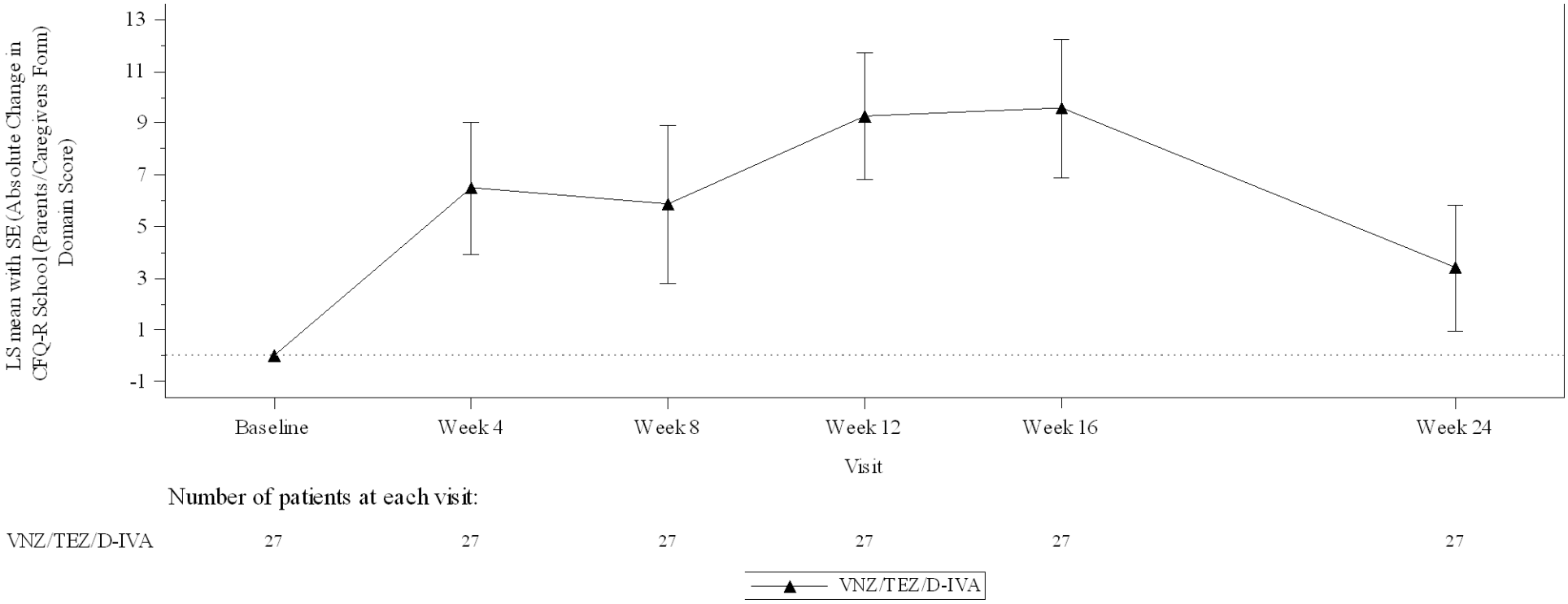

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Region = North America

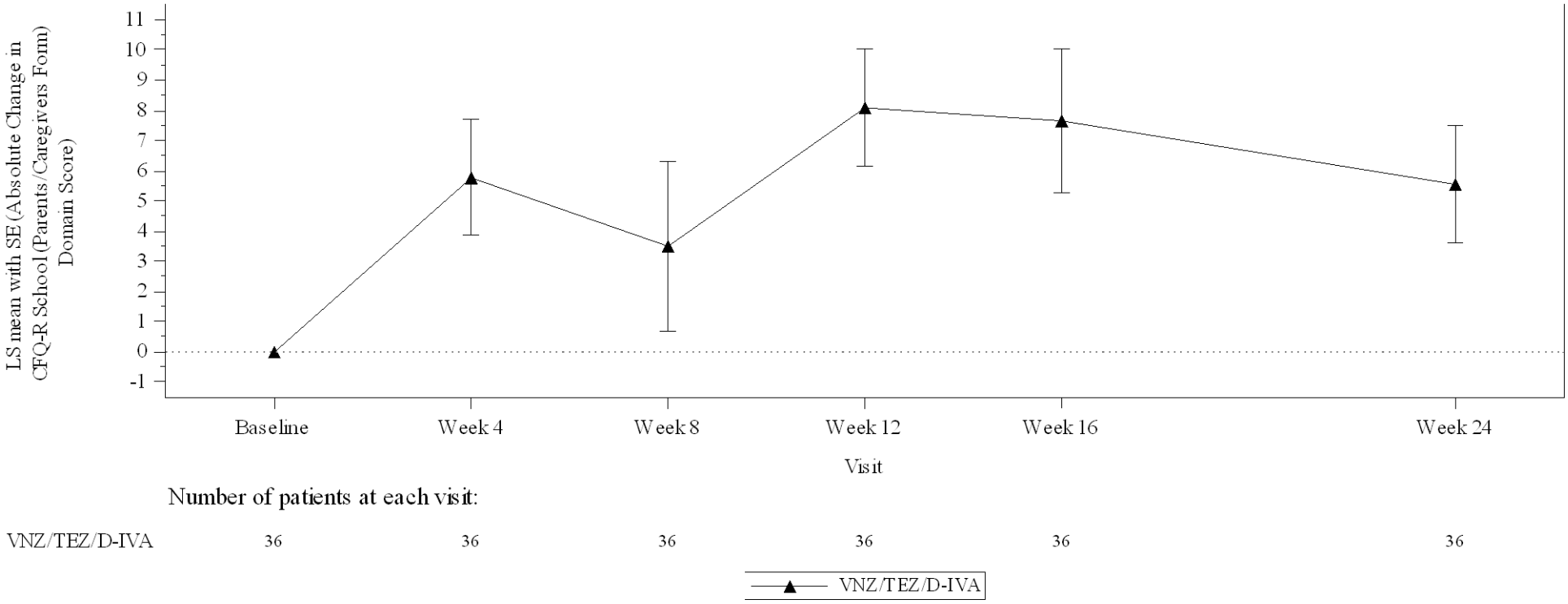

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Region = Rest of World

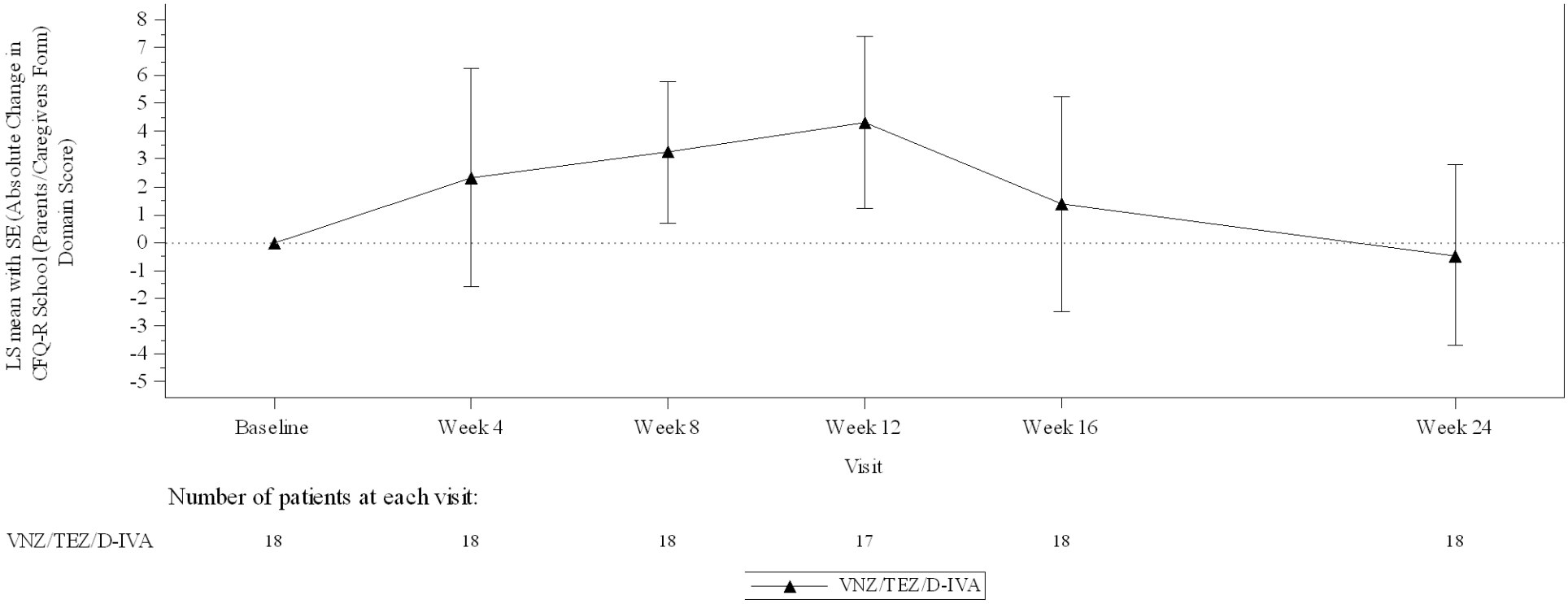

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

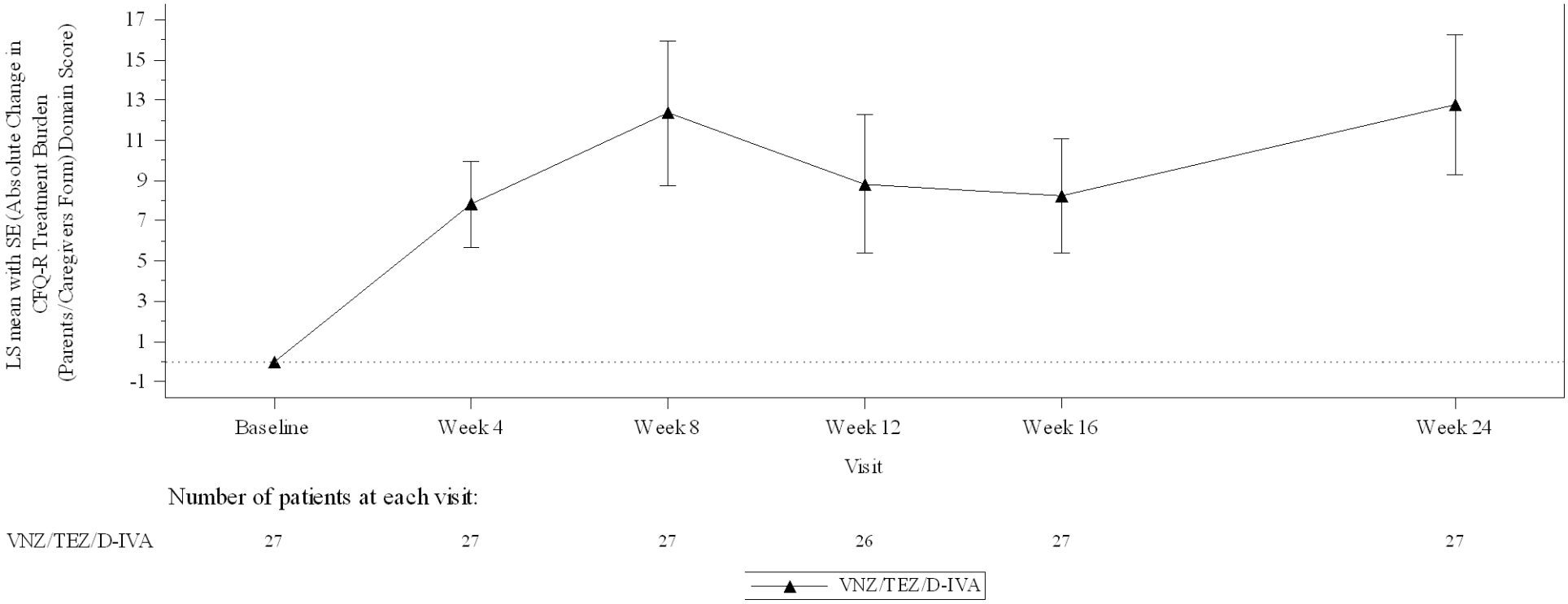

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

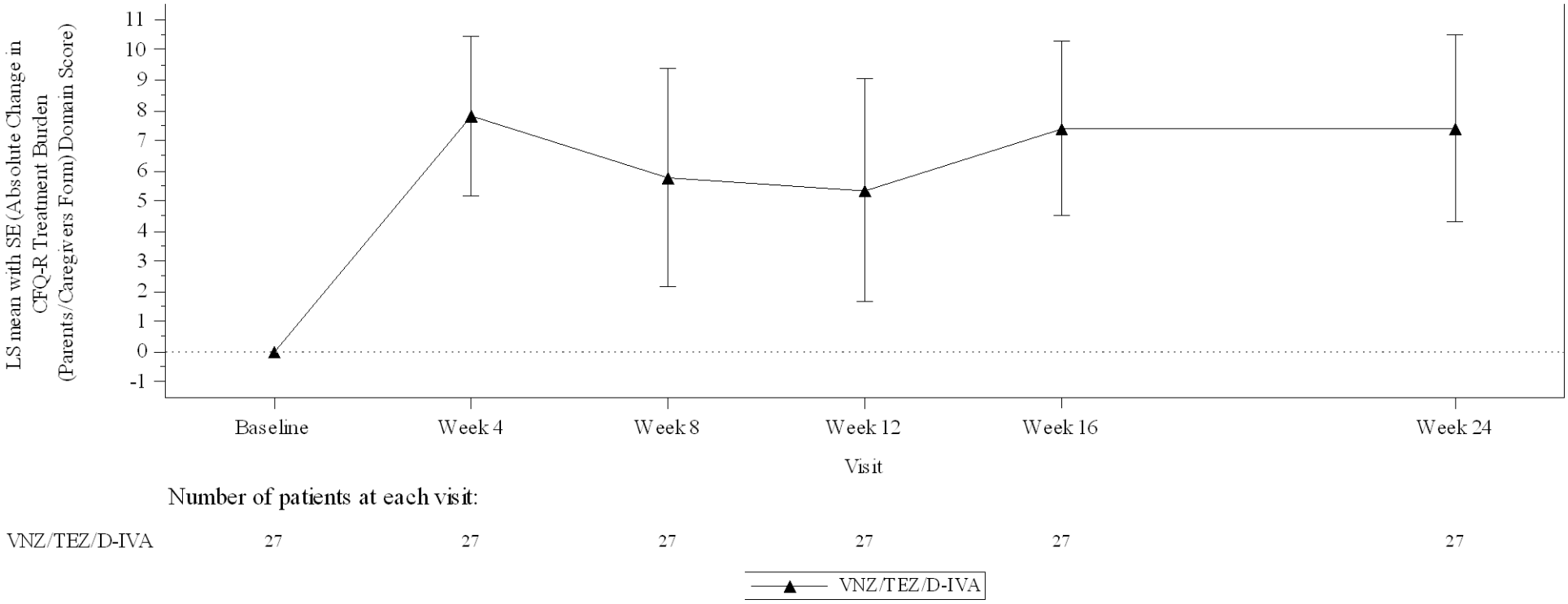

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

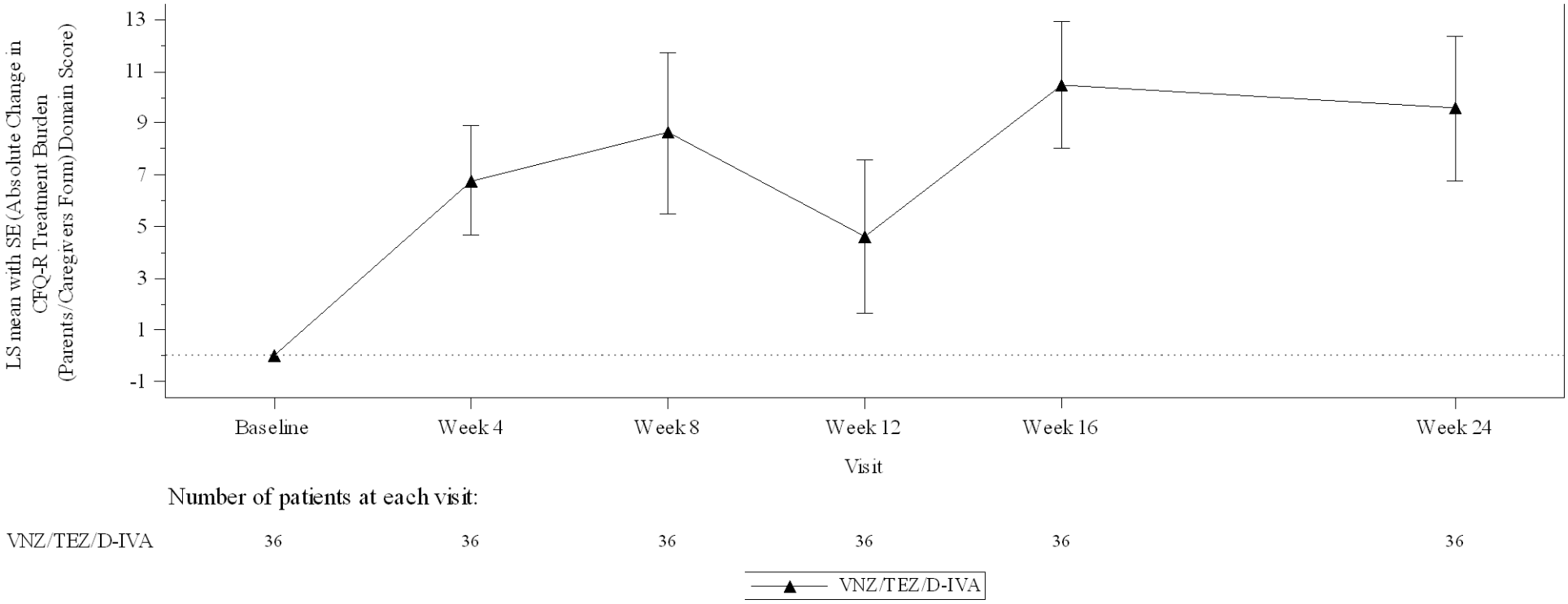

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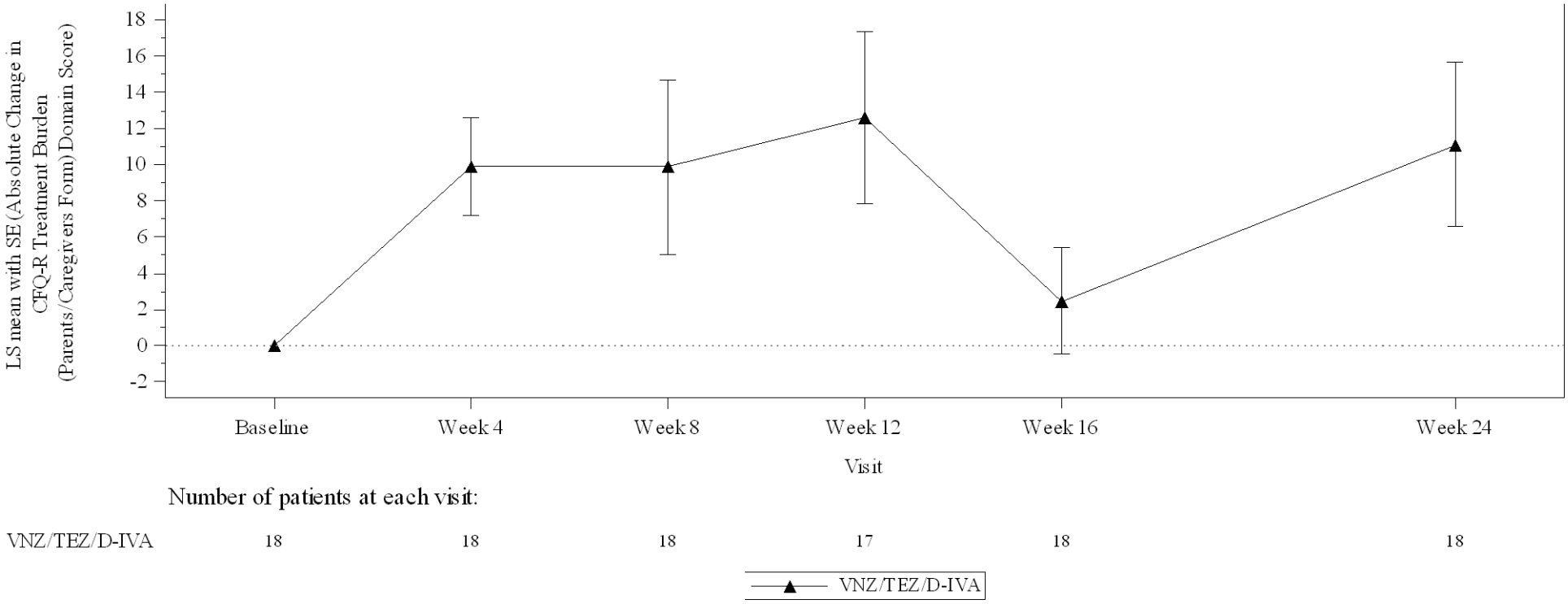
Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World



Number of patients at each visit:

	Baseline	Week 4	Week 8	Week 12	Week 16	Week 24
VNZ/TEZ/D-IVA	18	18	18	17	18	18

VNZ/TEZ/D-IVA

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Figure 2.2.2.10.6
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non-(F/MF)
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Sex = Male

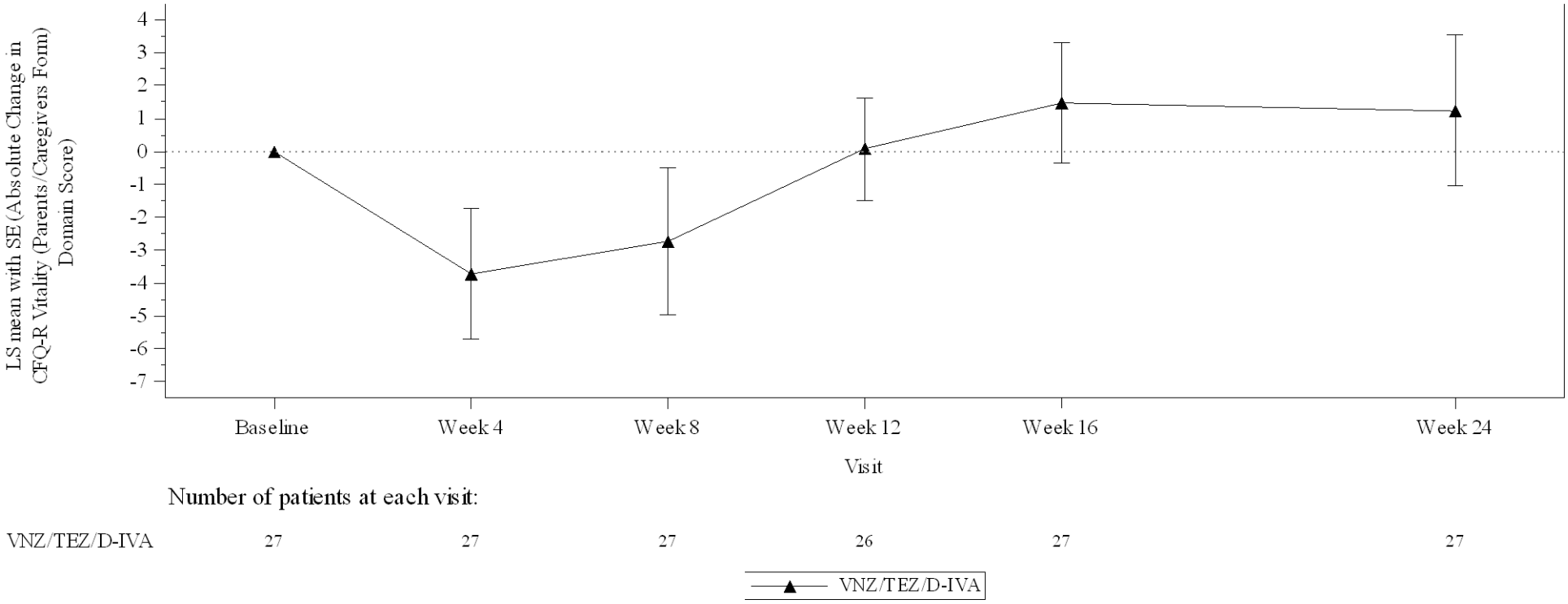

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Sex = Female

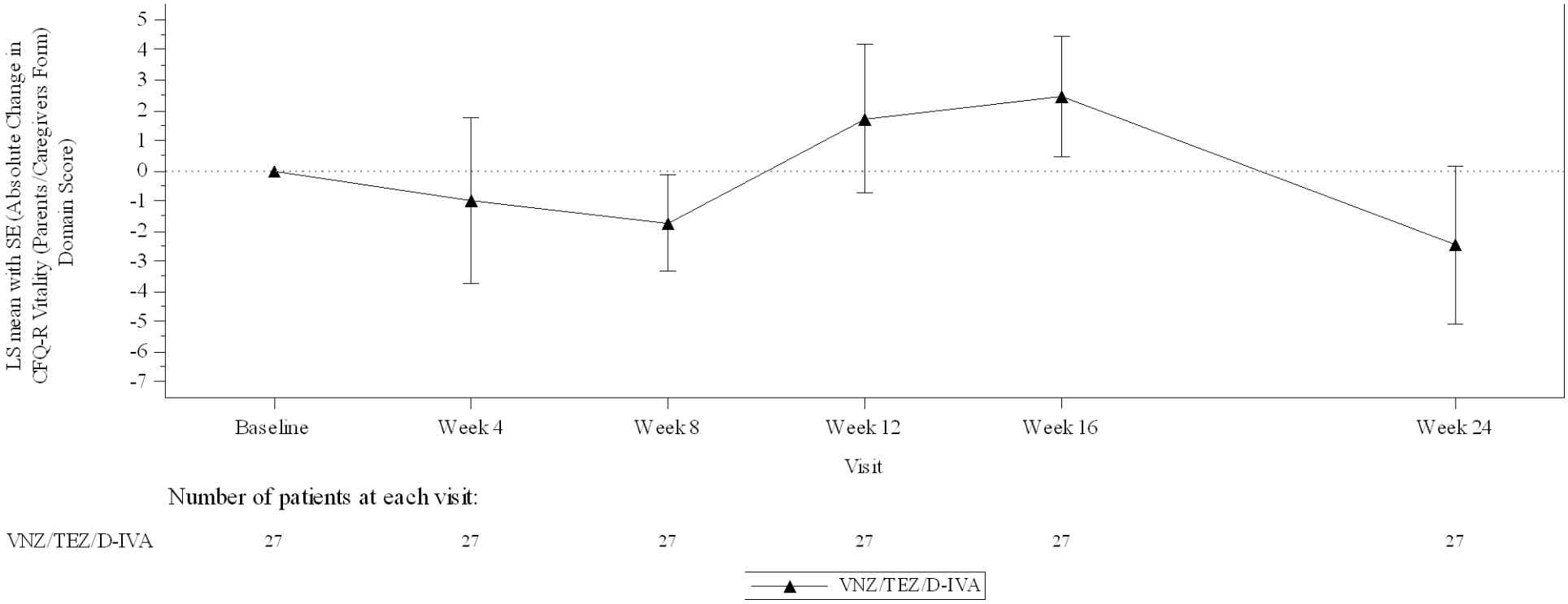

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Region = North America

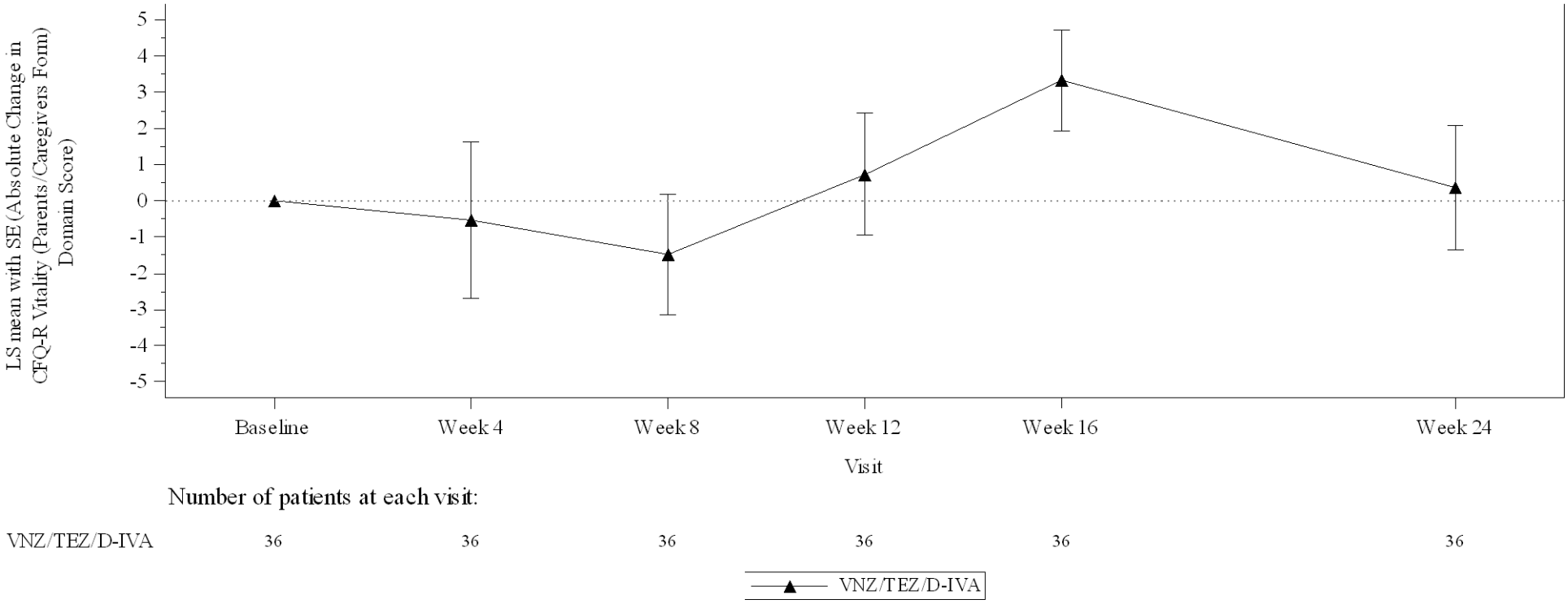

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

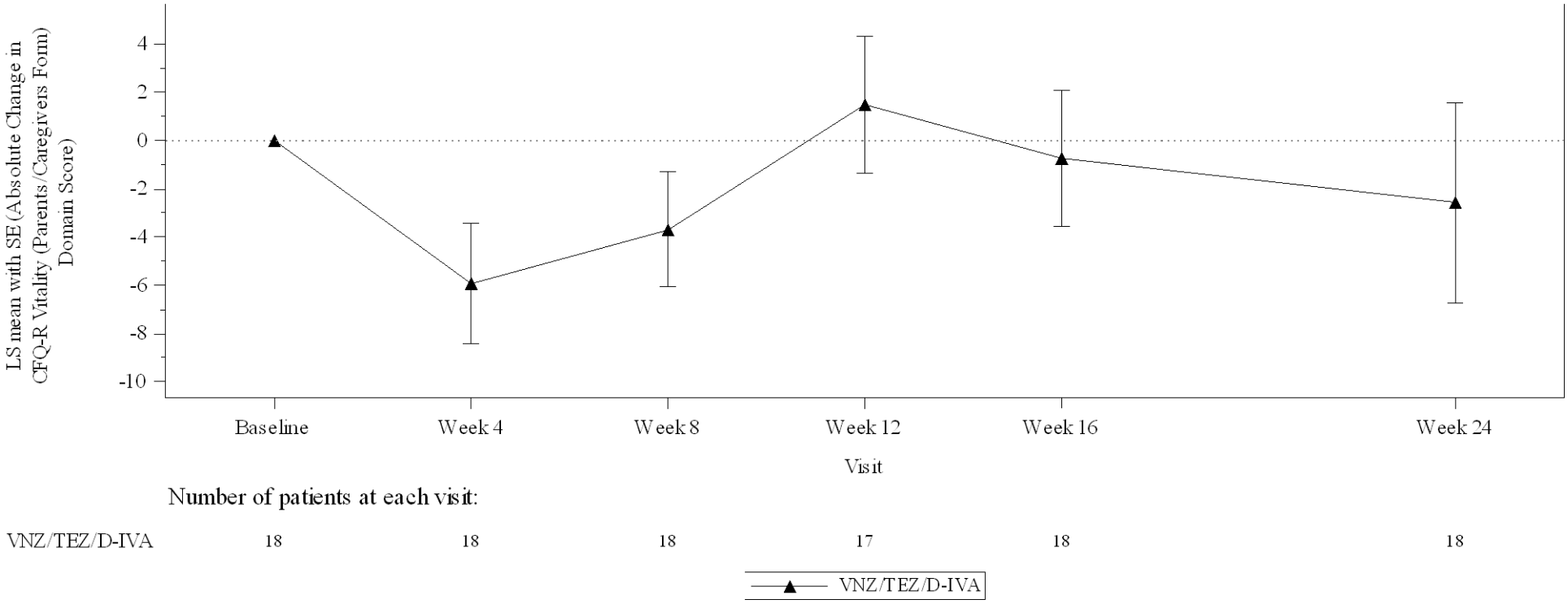

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Sex = Male

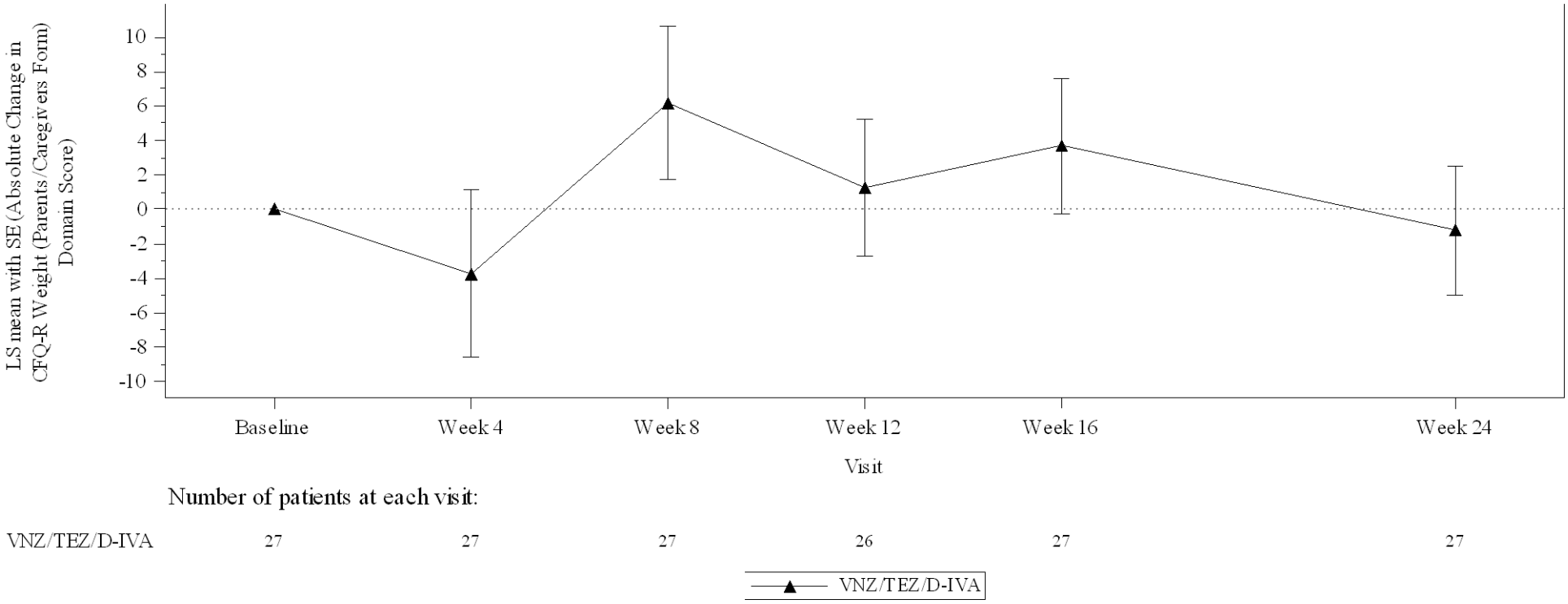

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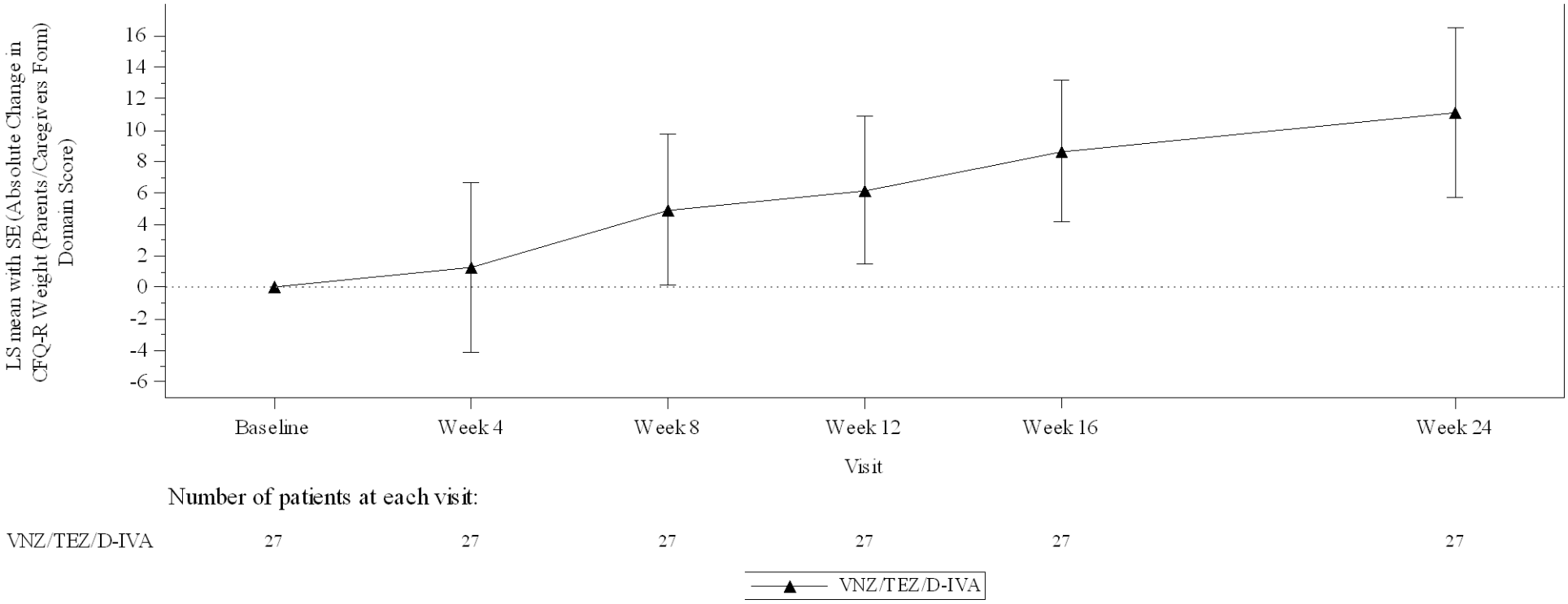
Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Sex = Female



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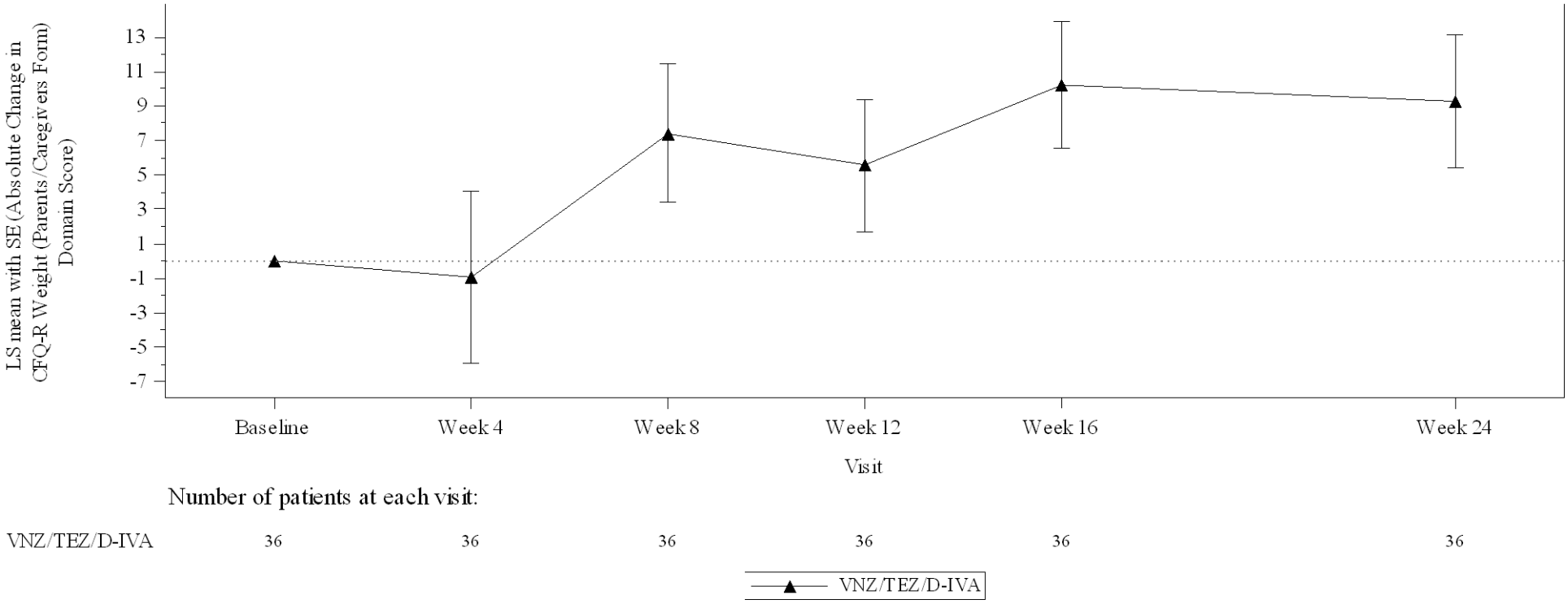
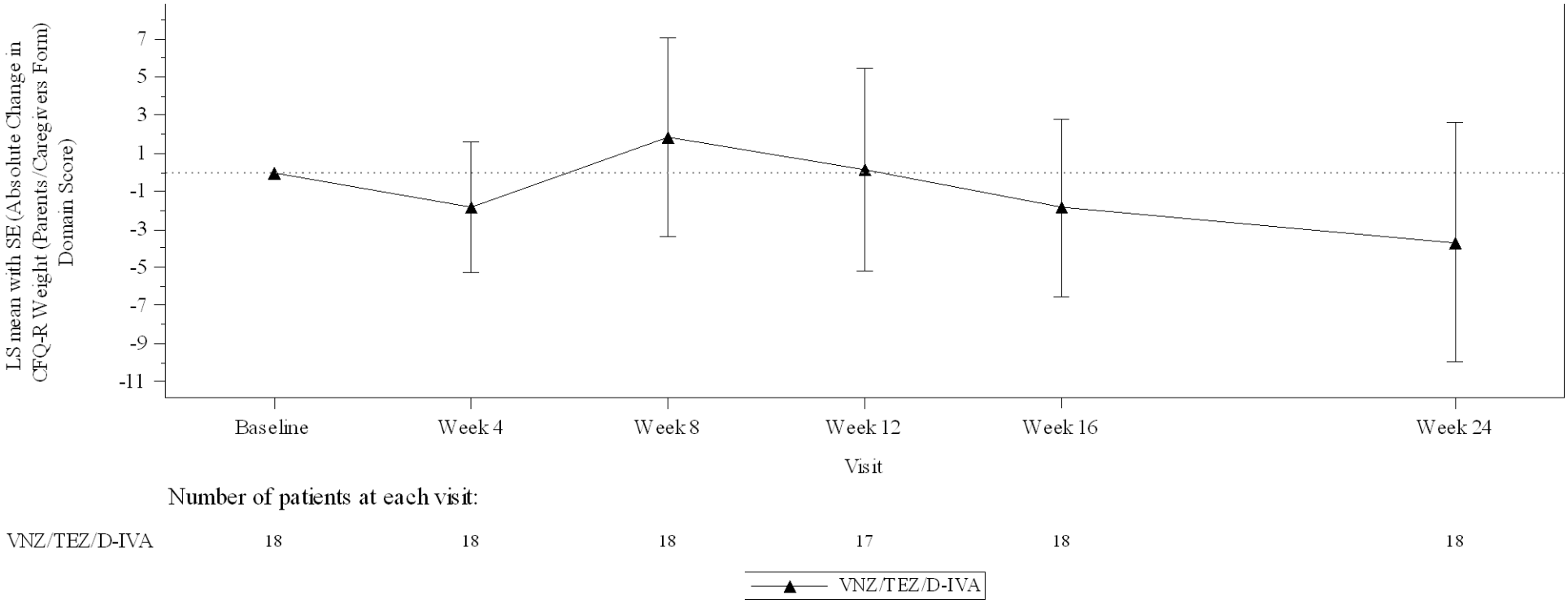
non-(F/MF)
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.14.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-km-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.14.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-km-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.14.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-km-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.14.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of the World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-km-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.14.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-km-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.14.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-km-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.15.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-hosp-km-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.15.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-hosp-km-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.15.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-hosp-km-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.15.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of the World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-hosp-km-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.15.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-hosp-km-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.15.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-hosp-km-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.16.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-iv-km-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.16.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-iv-km-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.16.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-iv-km-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.16.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of the World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-iv-km-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.16.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

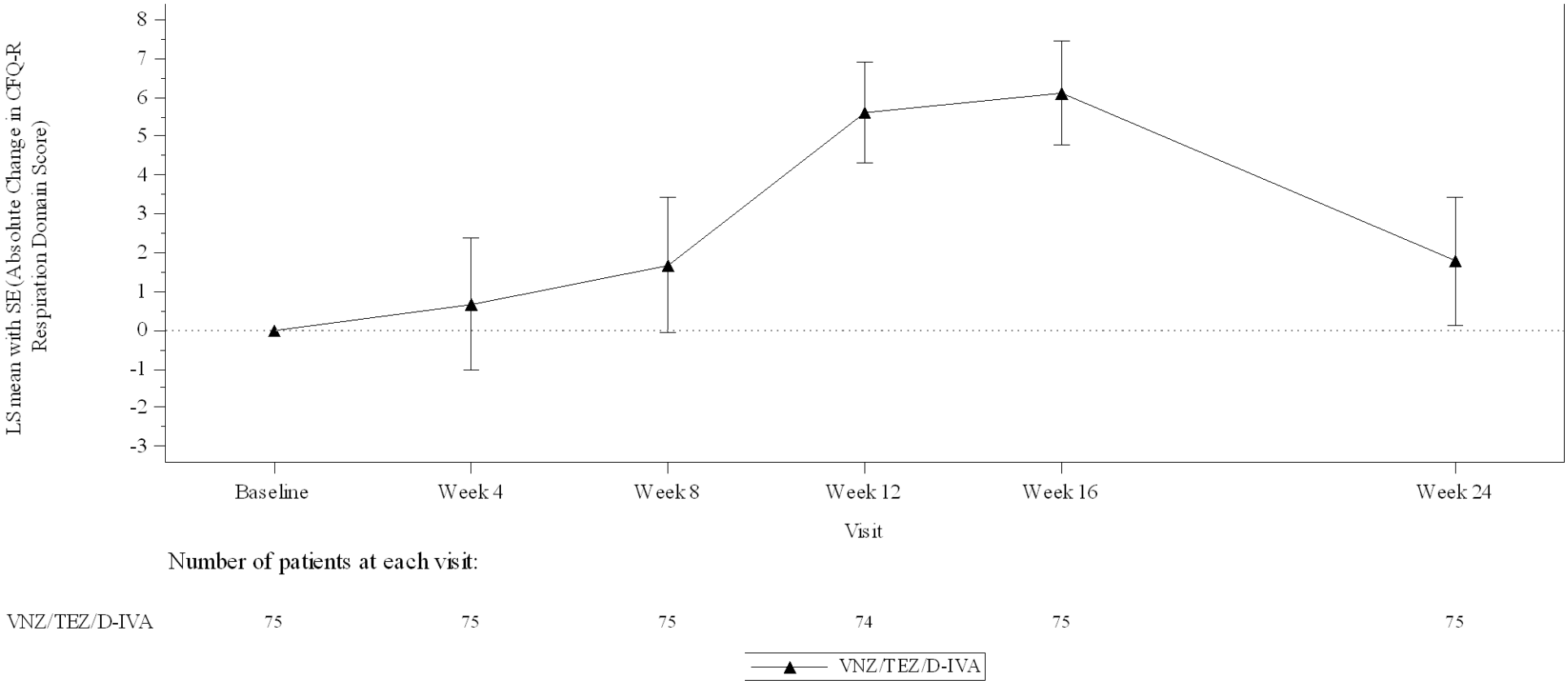
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-iv-km-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

Figure 2.2.2.16.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-iv-km-24wks-sub-b1-nonfmf.sas Creation: 06FEB2025 10:19

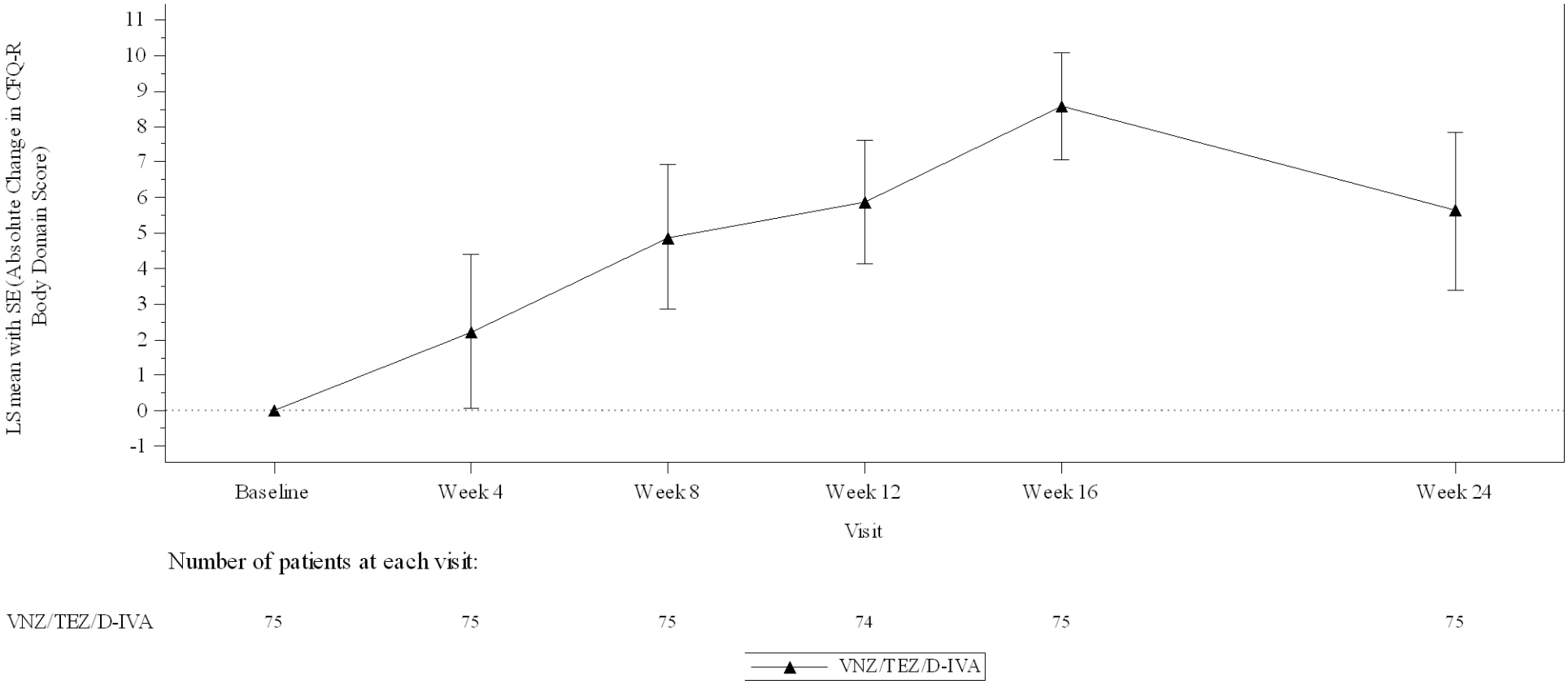
Figure 3.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Respiration



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1.sas Creation: 06FEB2025 10:19

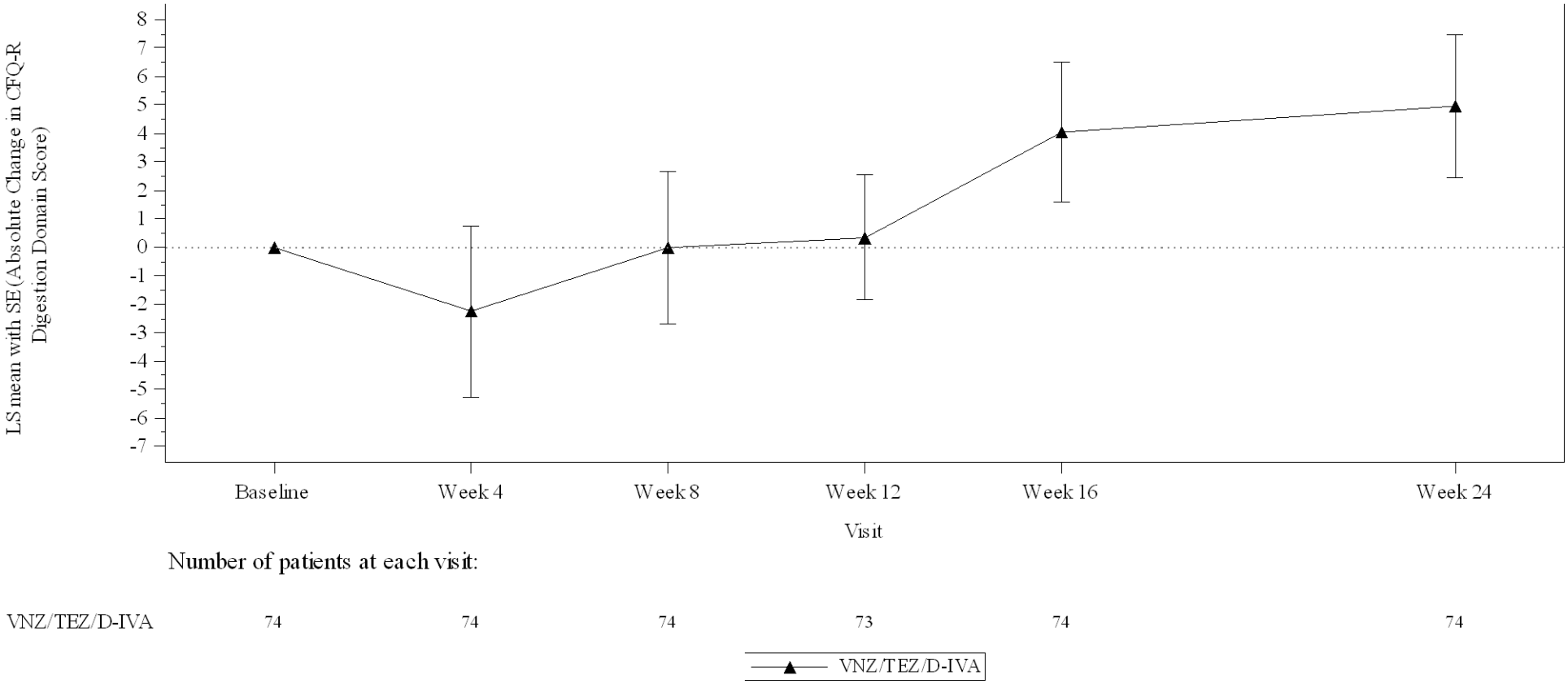
Figure 3.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Body



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1.sas Creation: 06FEB2025 10:19

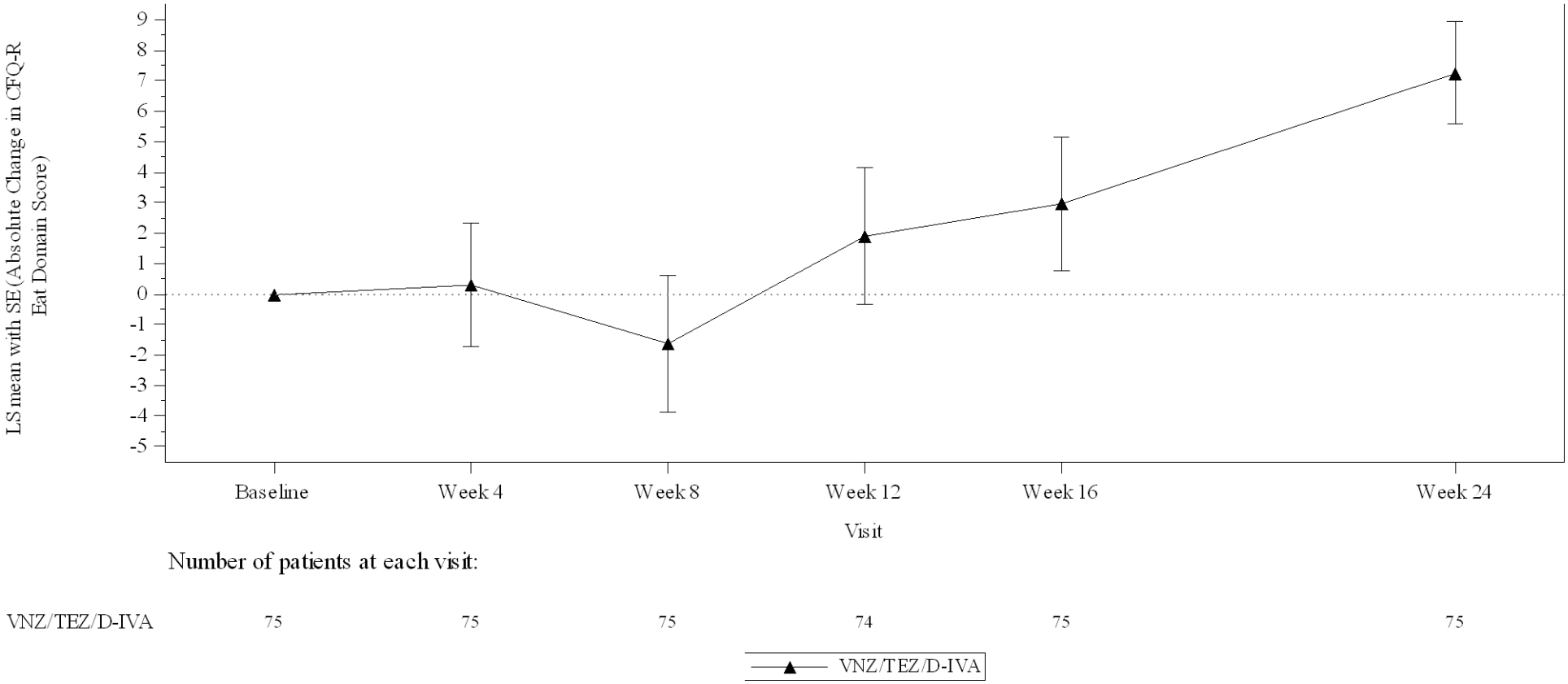
Figure 3.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Digestion



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1.sas Creation: 06FEB2025 10:19

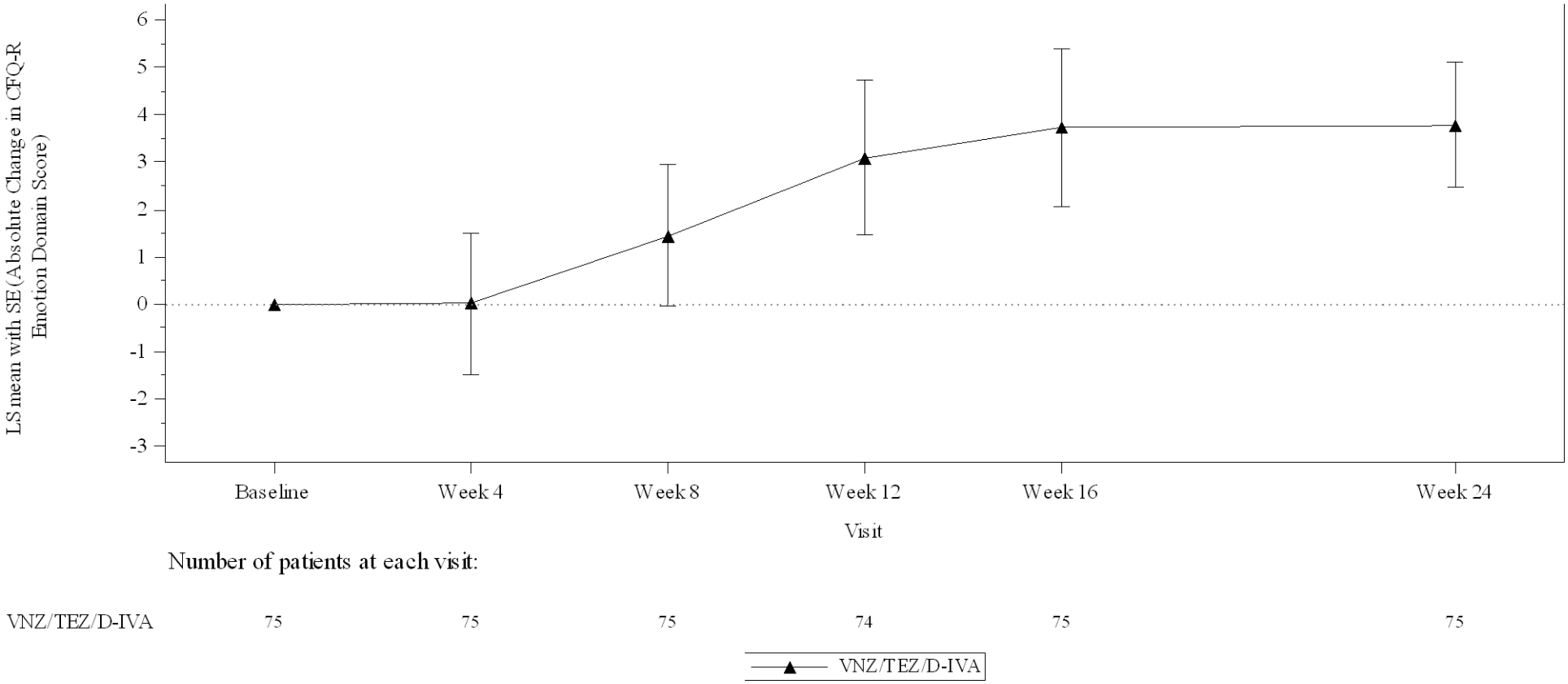
Figure 3.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Eat



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1.sas Creation: 06FEB2025 10:19

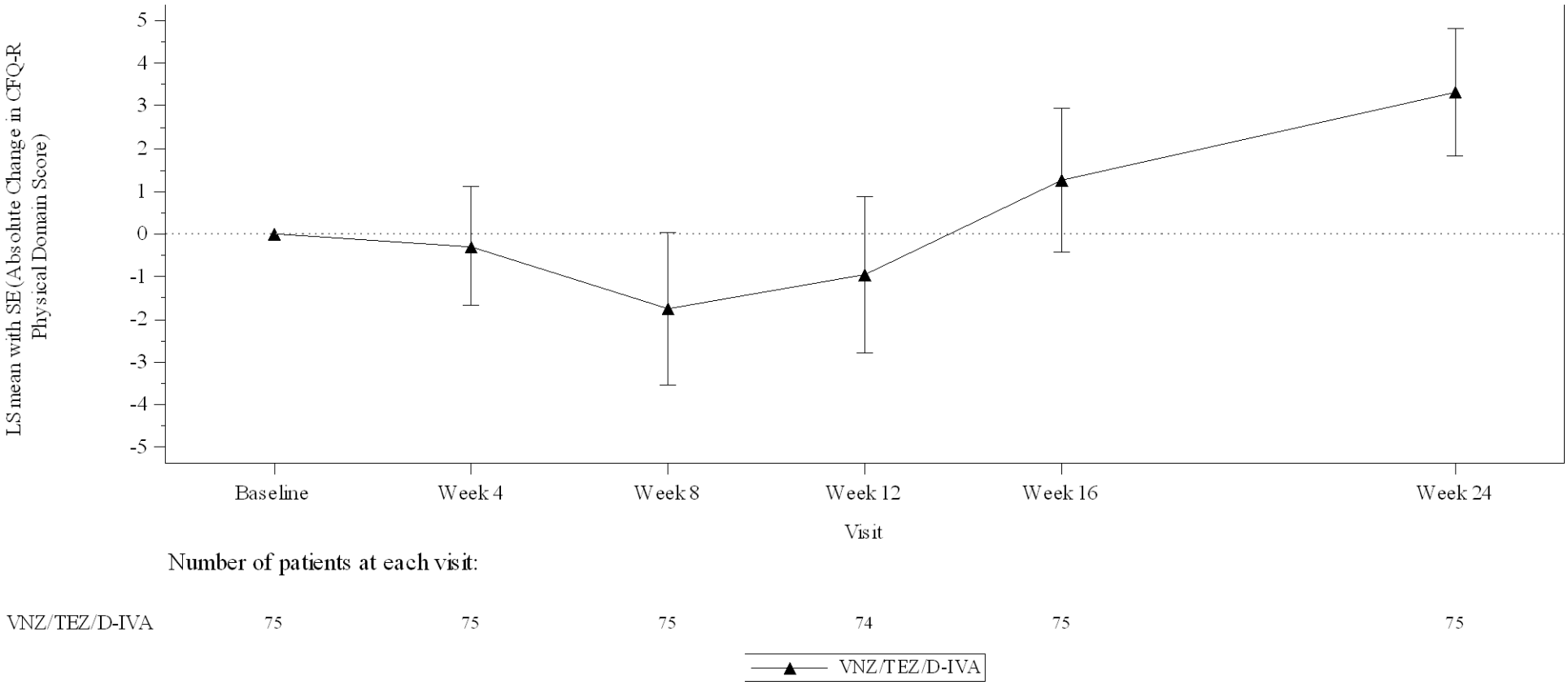
Figure 3.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Emotion



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1.sas Creation: 06FEB2025 10:19

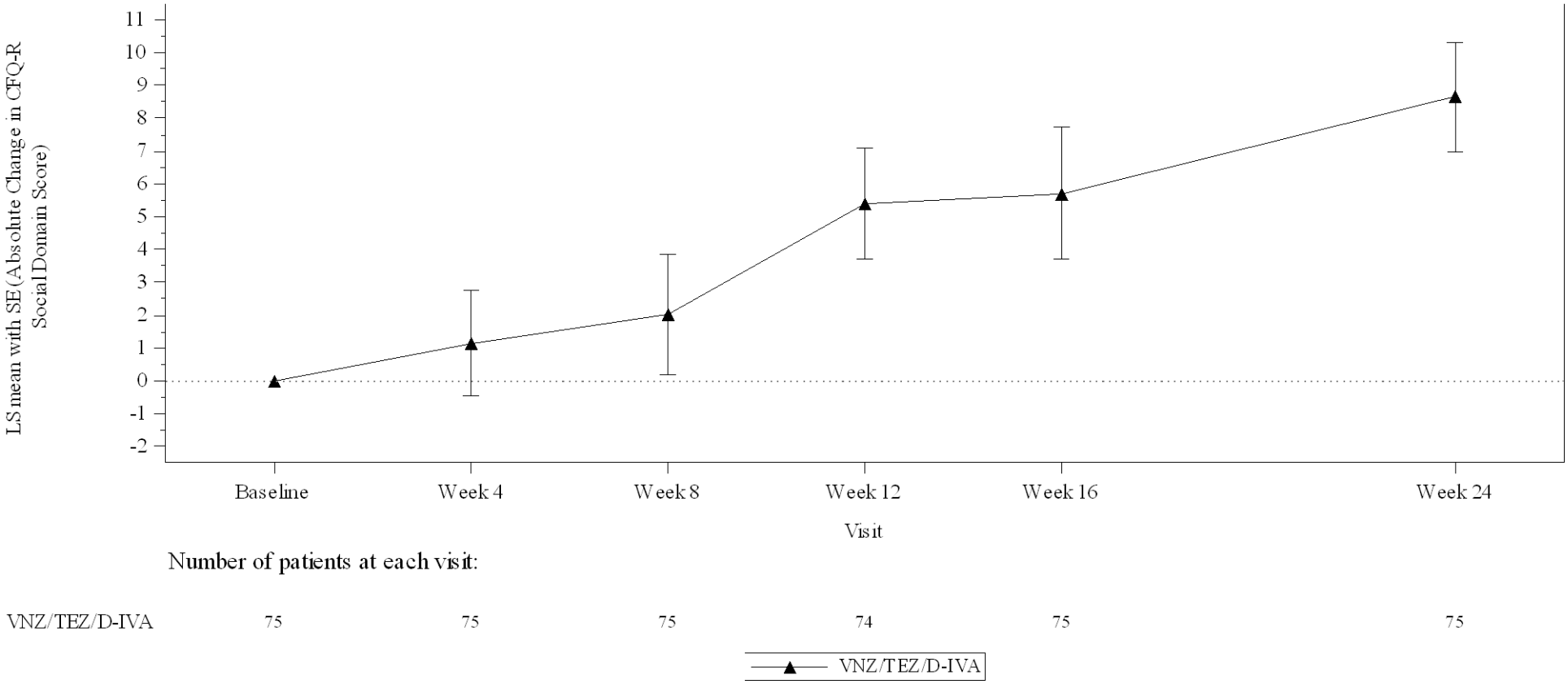
Figure 3.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Physical



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1.sas Creation: 06FEB2025 10:19

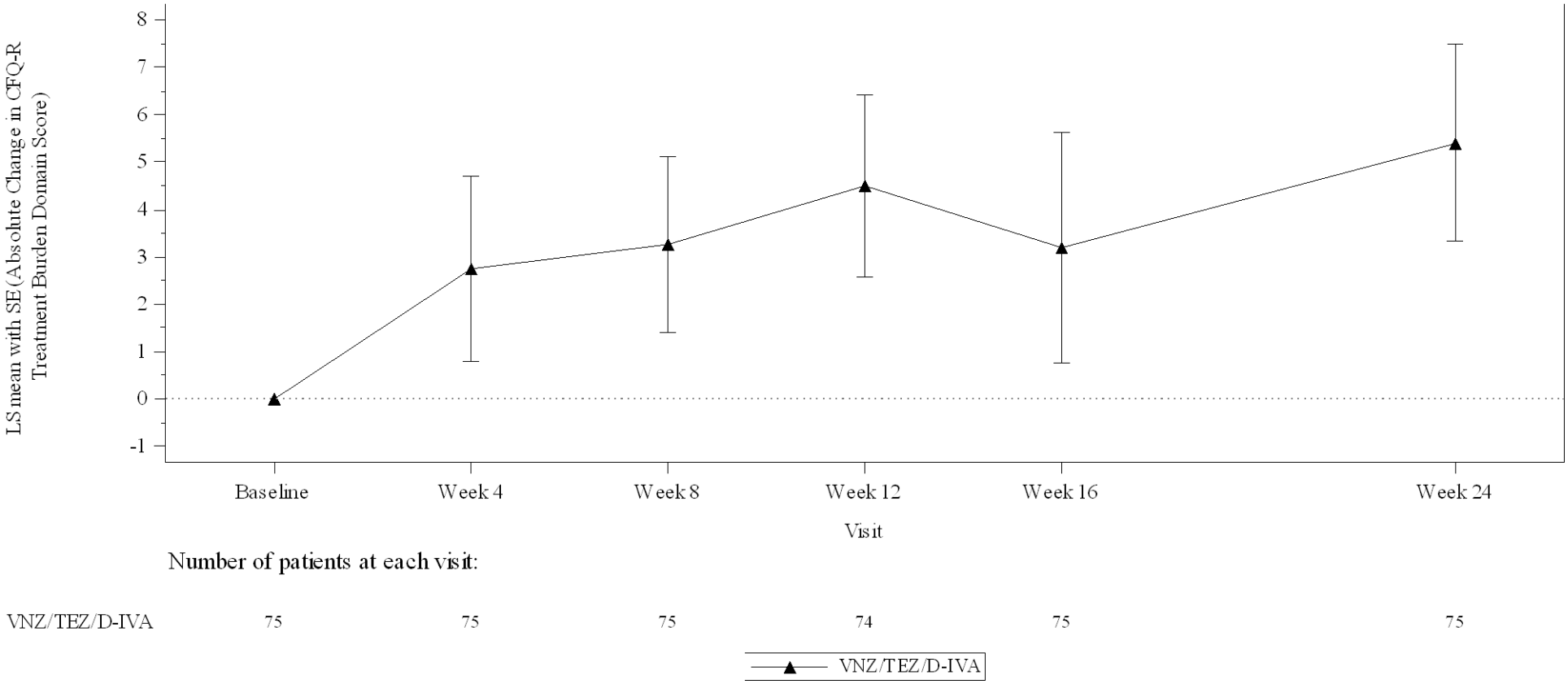
Figure 3.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Social



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1.sas Creation: 06FEB2025 10:19

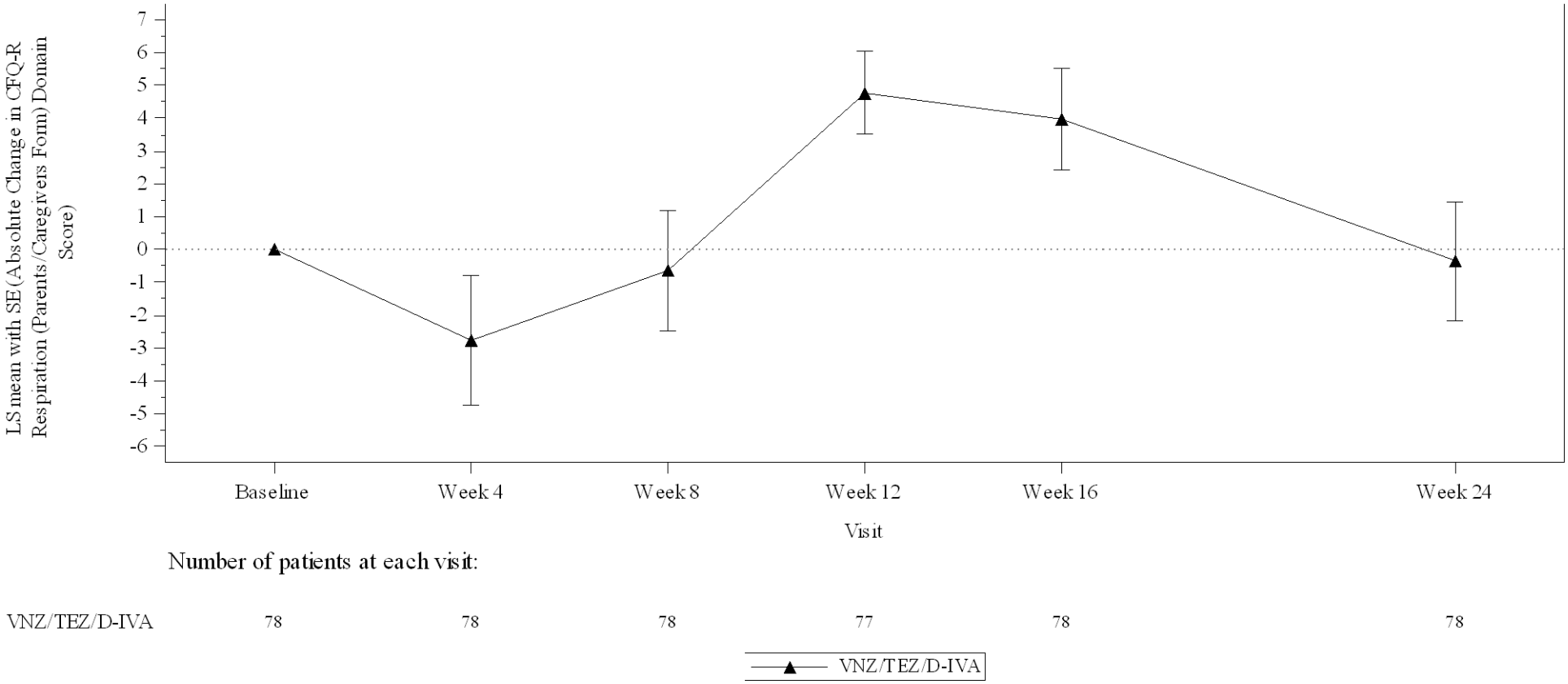
Figure 3.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Treatment Burden



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-b1.sas Creation: 06FEB2025 10:19

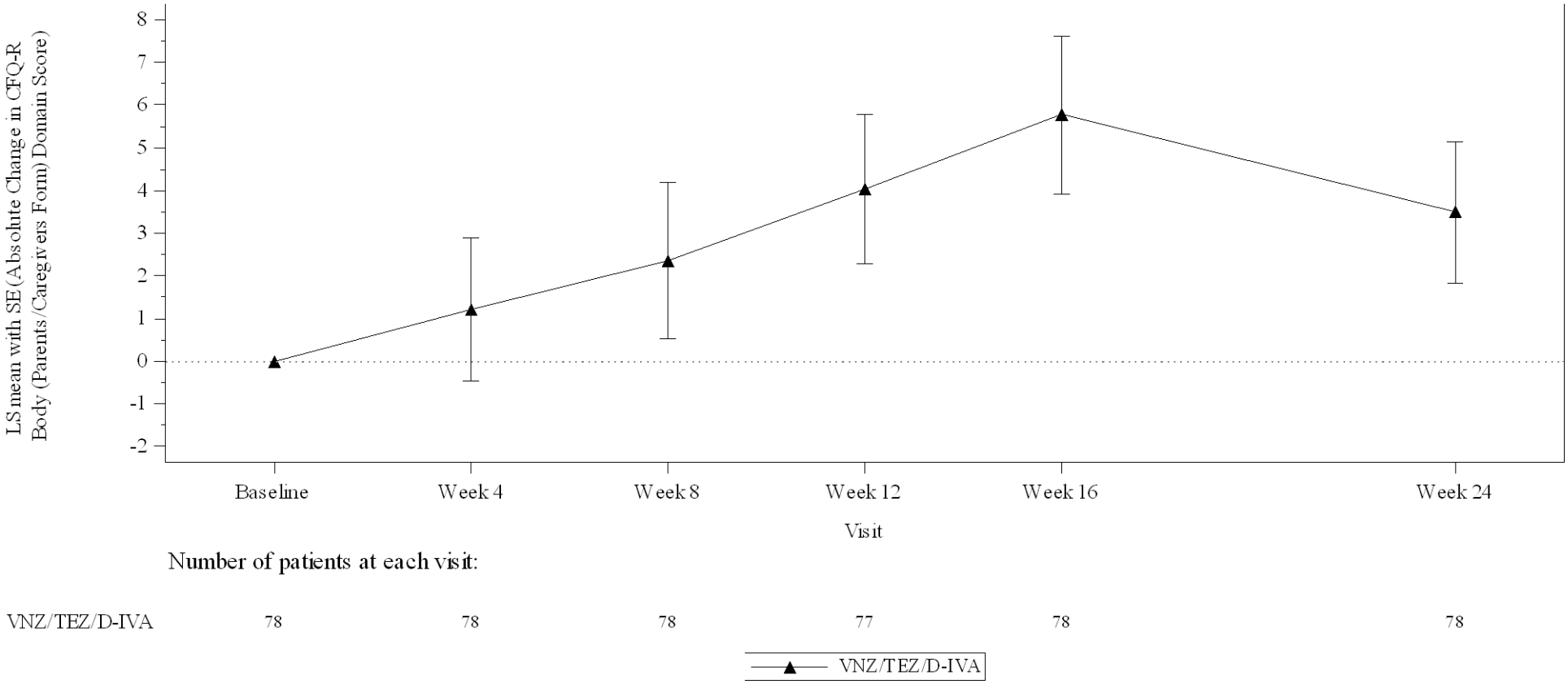
Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

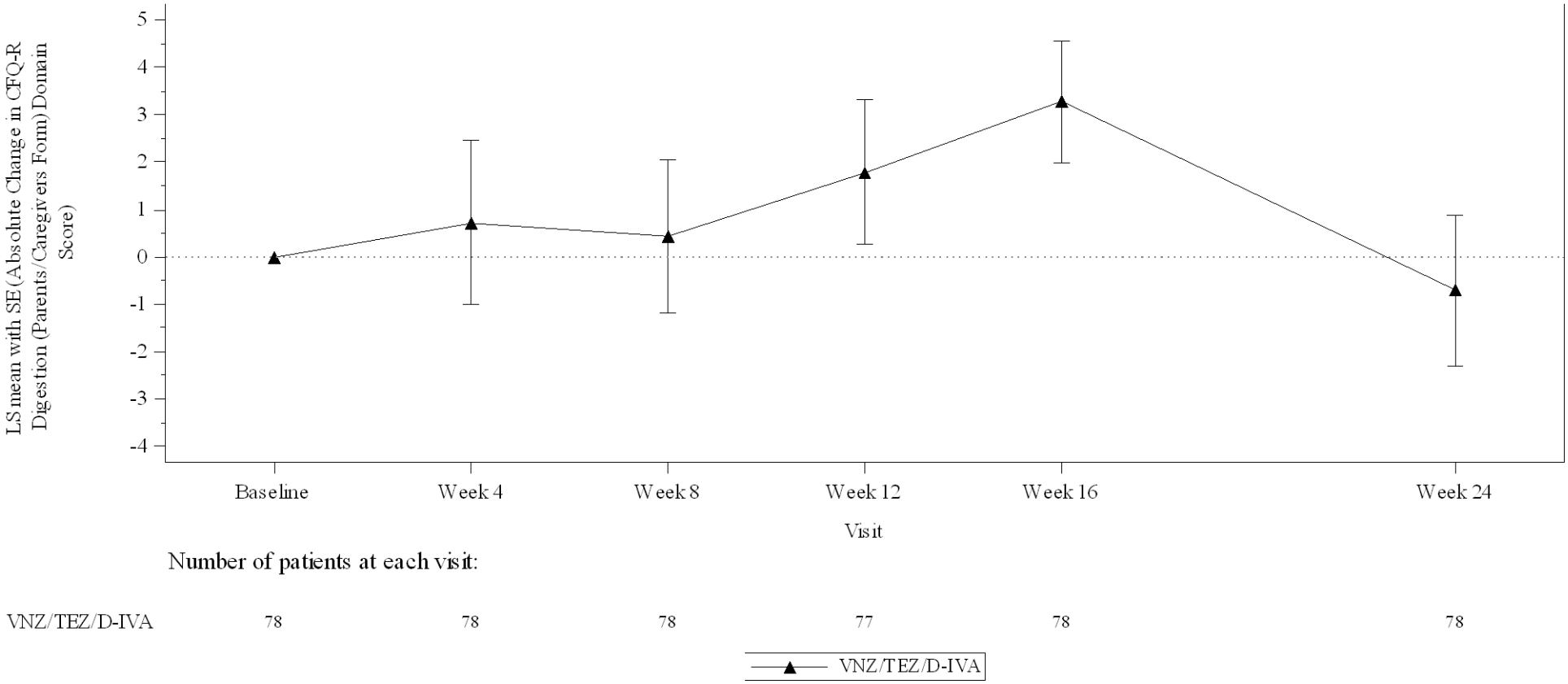
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1.sas Creation: 06FEB2025 10:20

Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Body (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

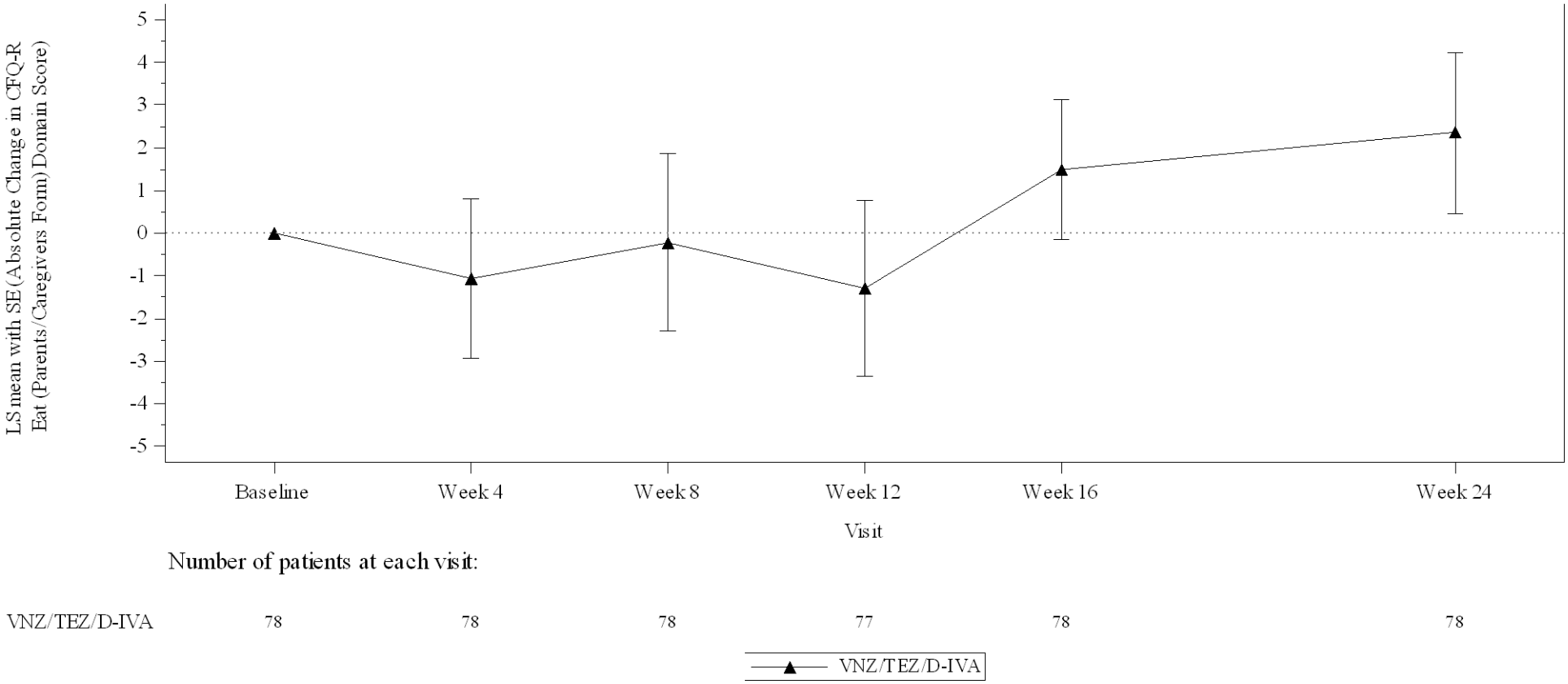
Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1.sas
Creation: 06FEB2025 10:20

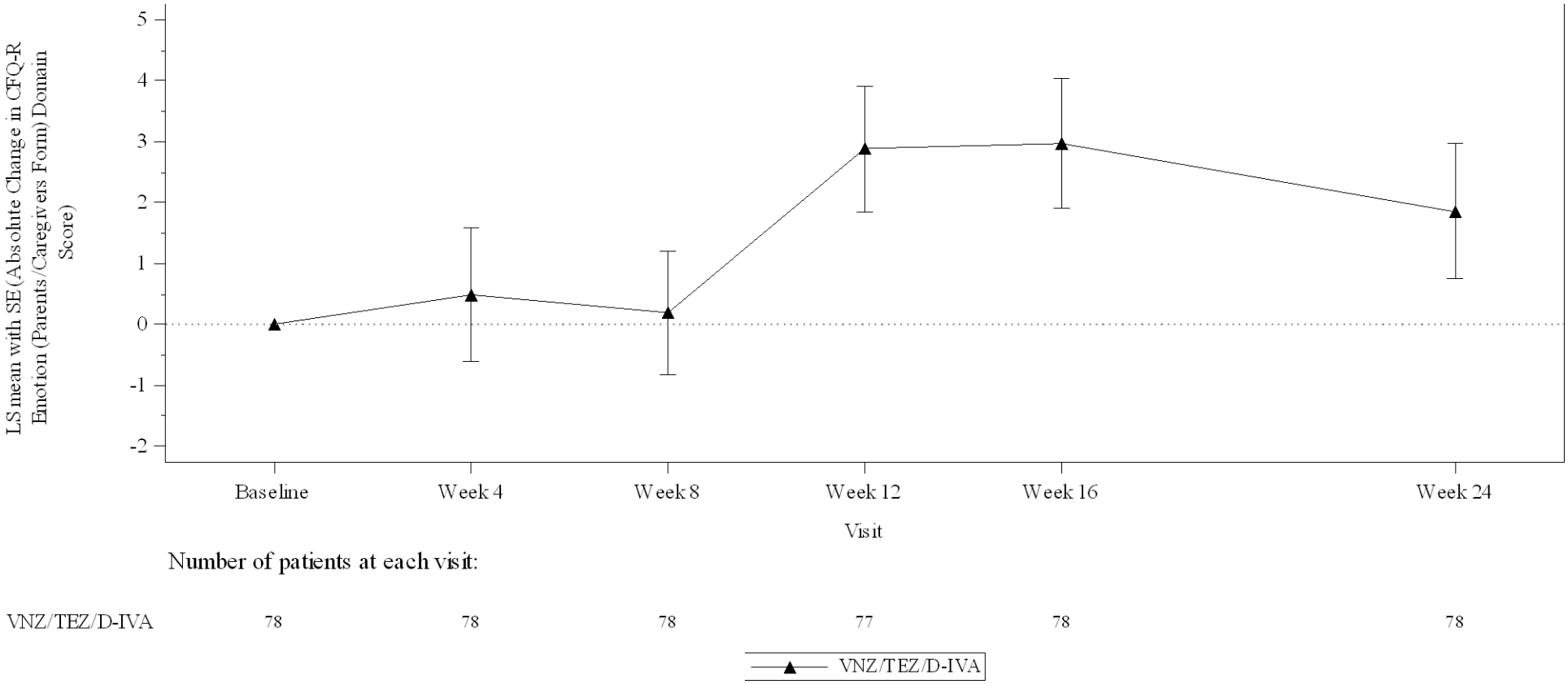
Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

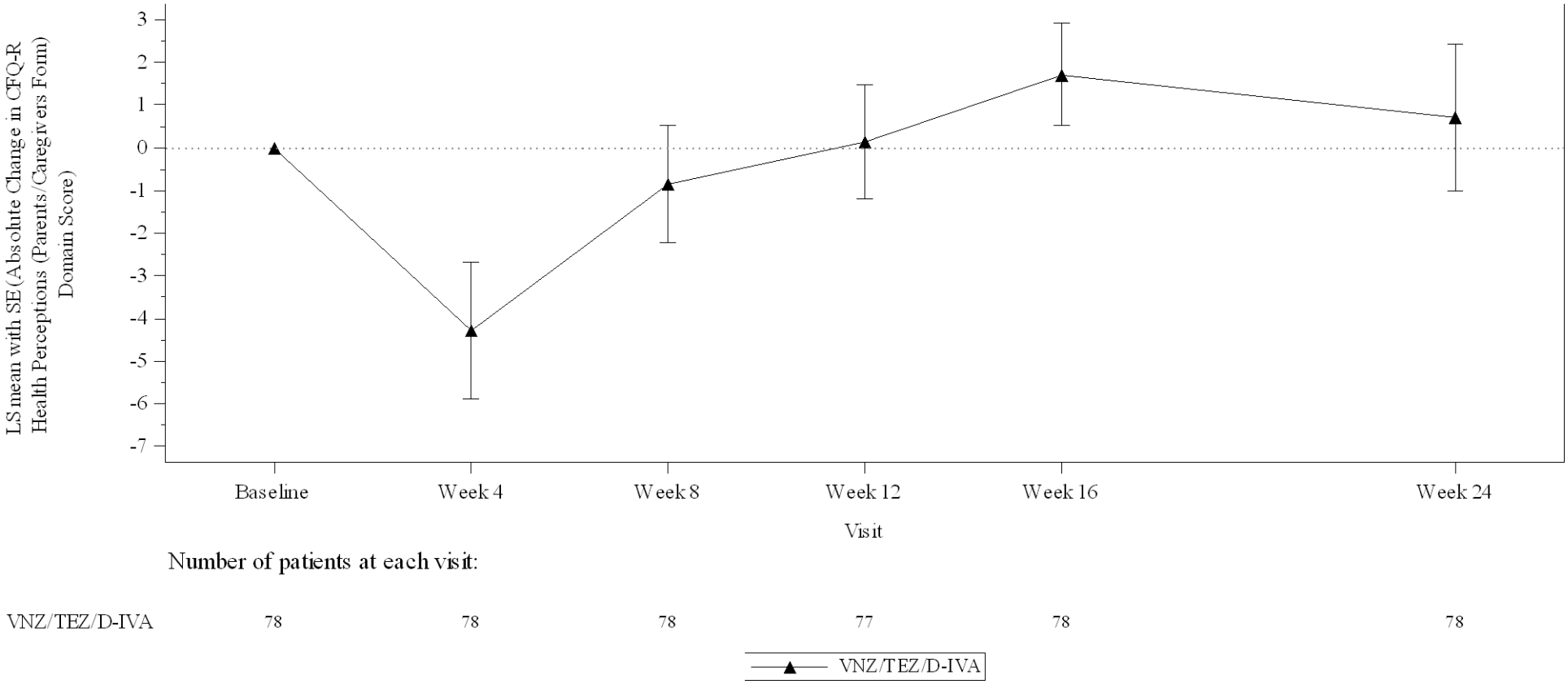
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1.sas Creation: 06FEB2025 10:20

Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

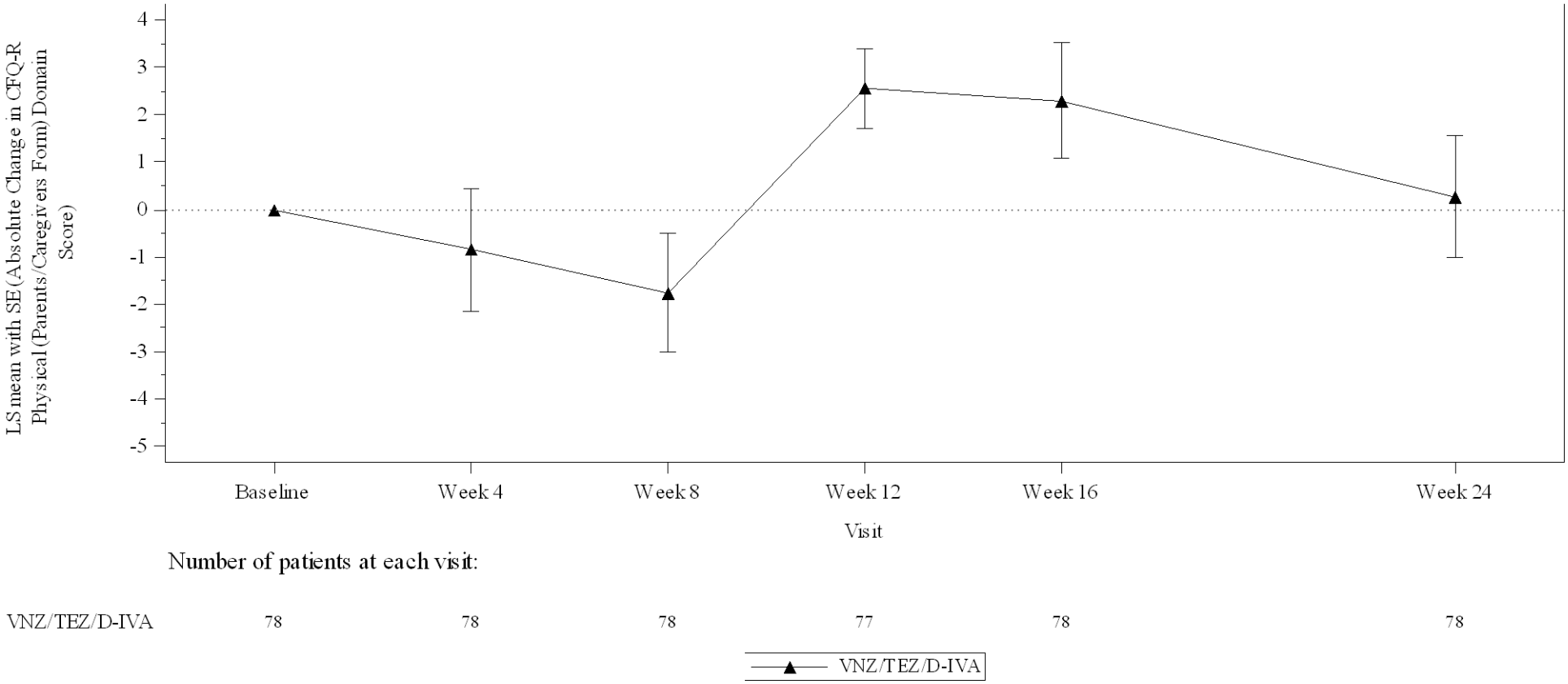
Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1.sas Creation: 06FEB2025 10:20

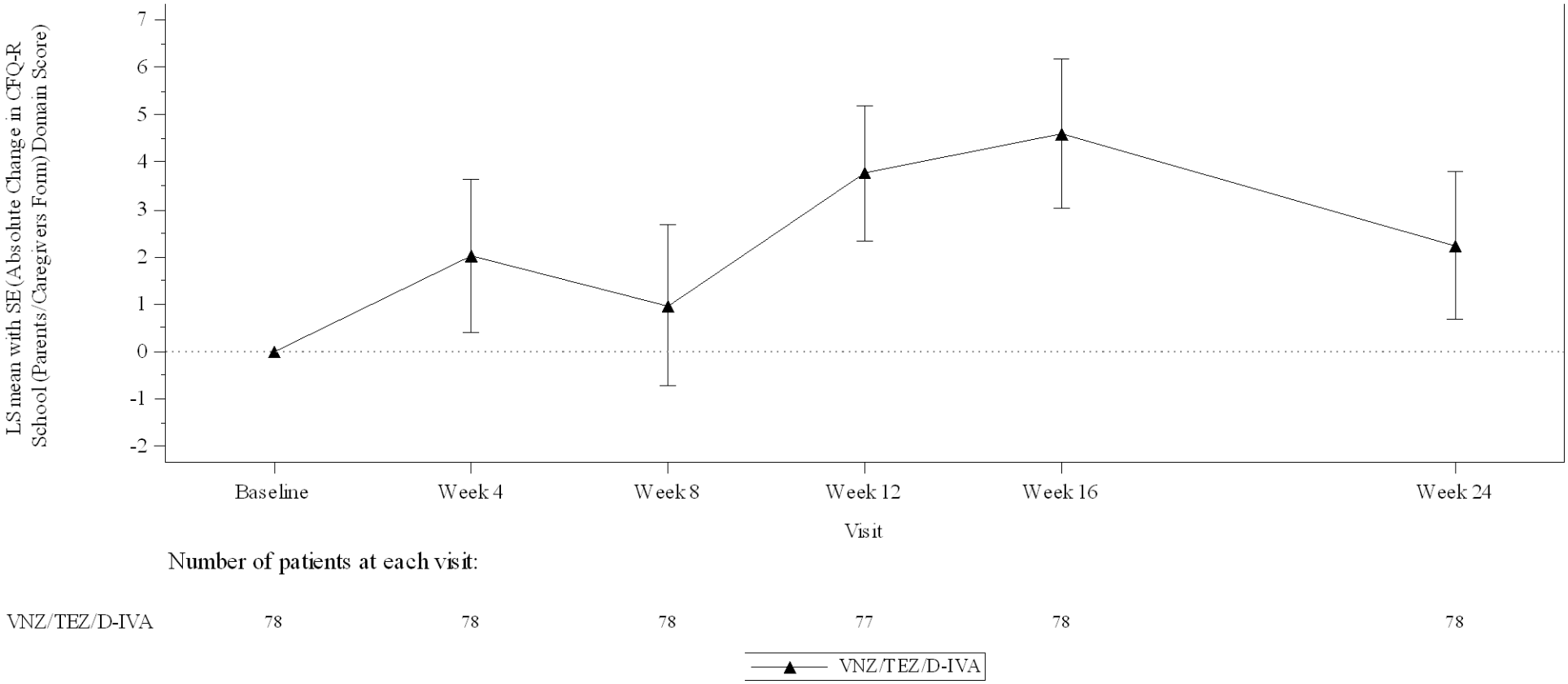
Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1.sas Creation: 06FEB2025 10:20

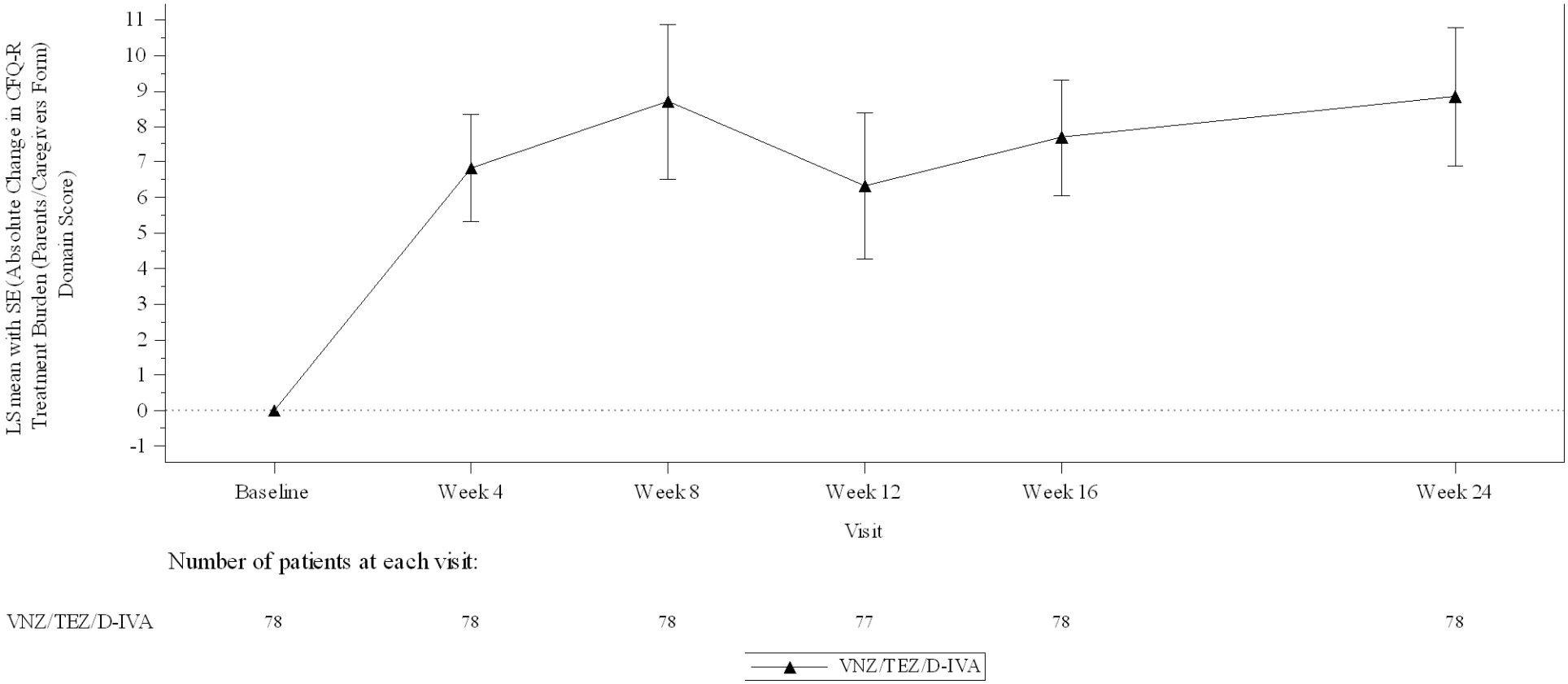
Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: School (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1.sas Creation: 06FEB2025 10:20

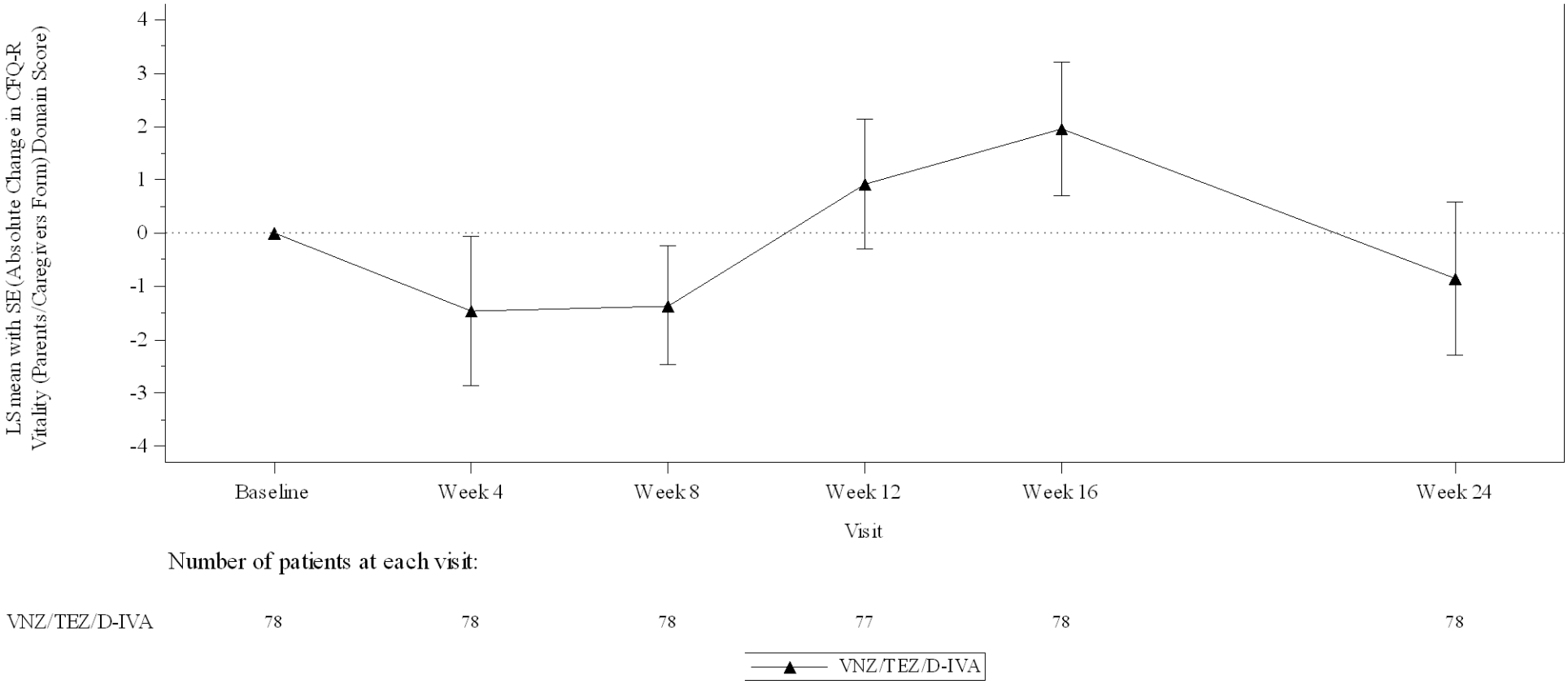
Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1.sas Creation: 06FEB2025 10:20

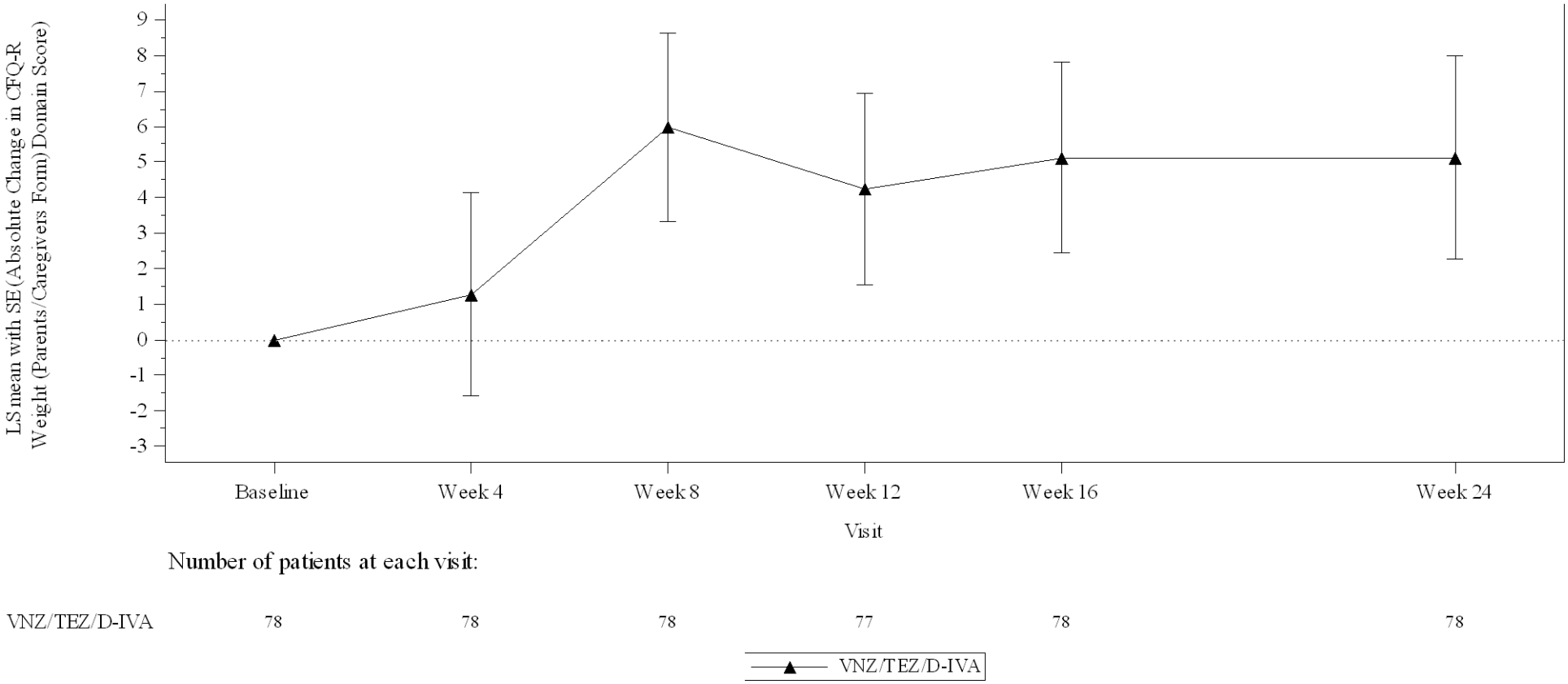
Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1.sas Creation: 06FEB2025 10:20

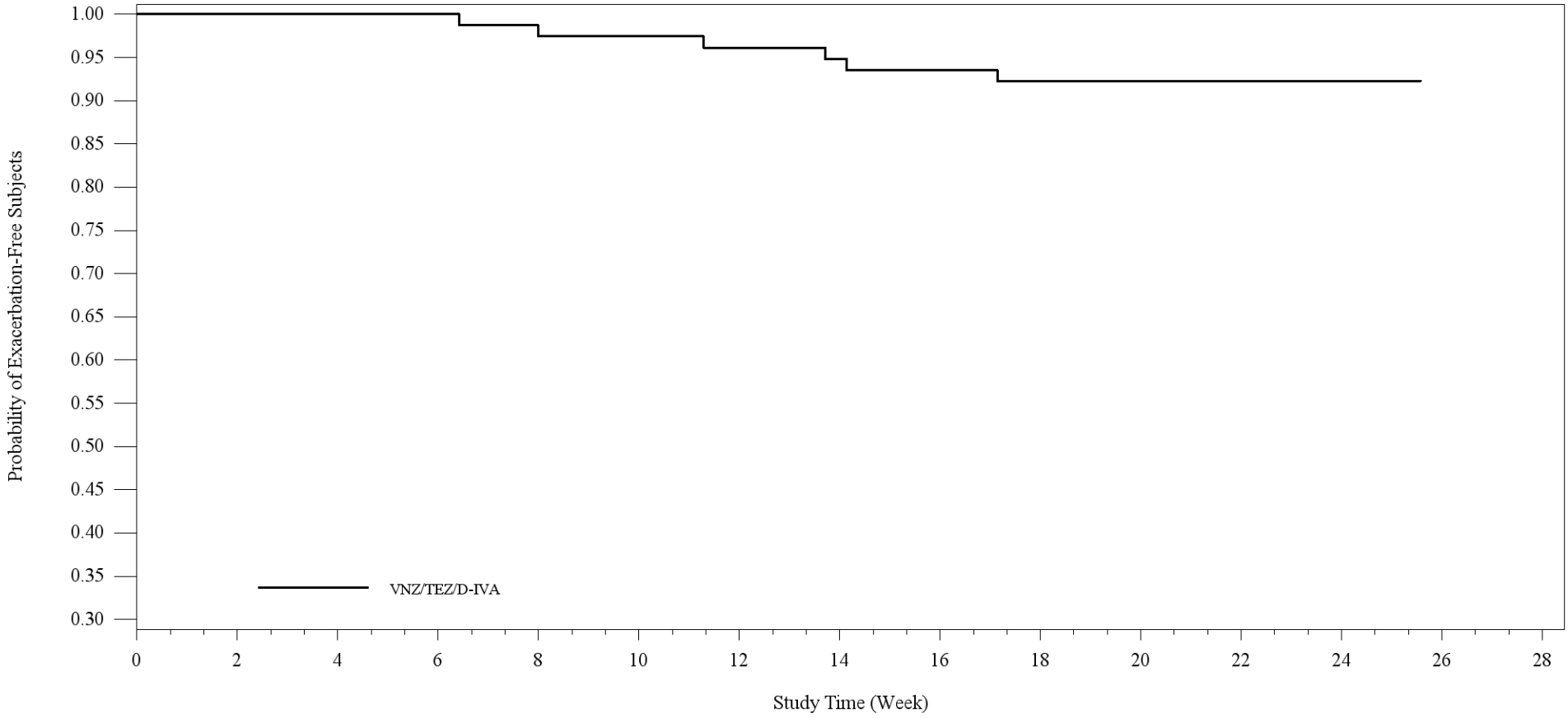
Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-b1.sas Creation: 06FEB2025 10:20

Figure 3.2.1.14.2
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 24
Full Analysis Set

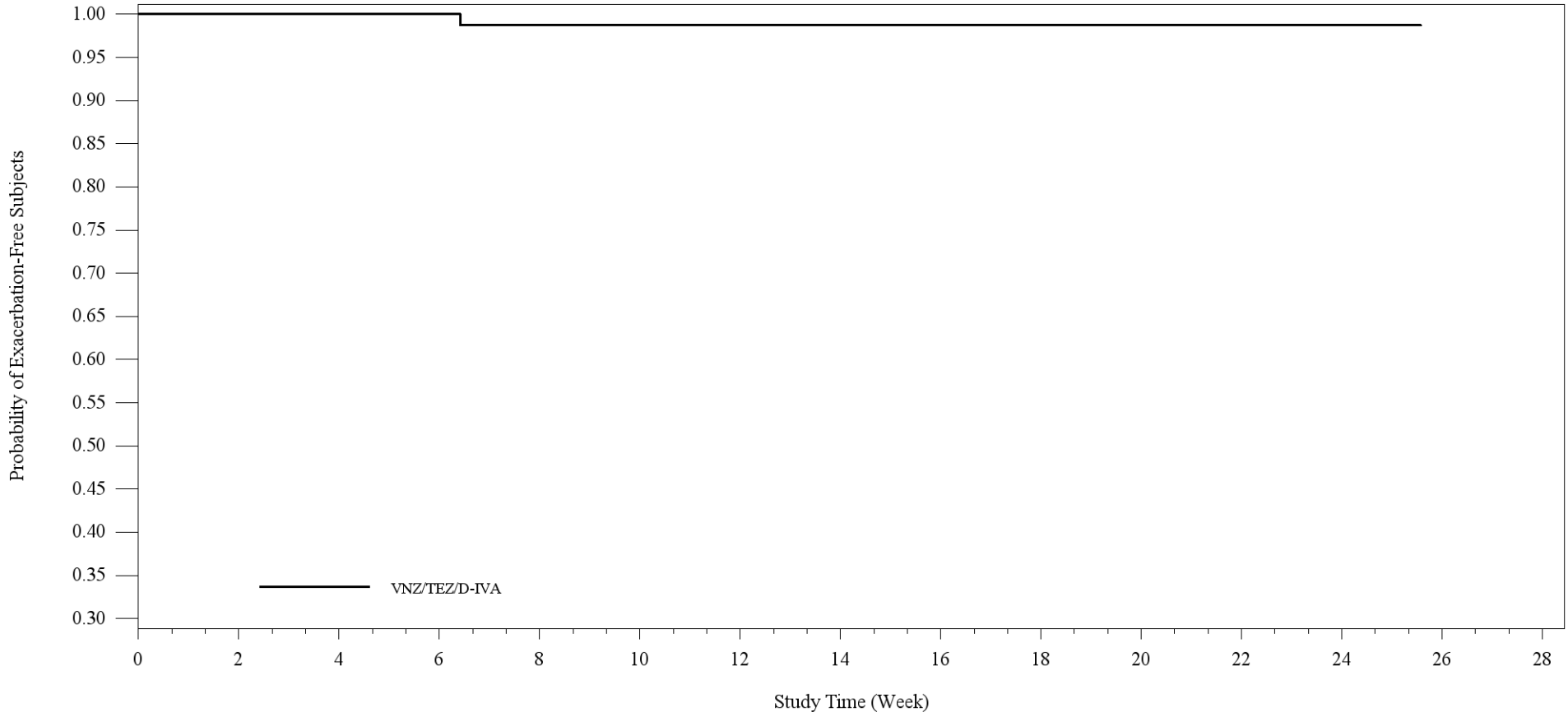


Number of Patients at Risk

VNZ/TEZ/D-IVA	78	78	76	75	73	44

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 3.2.1.15.2
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 24
Full Analysis Set

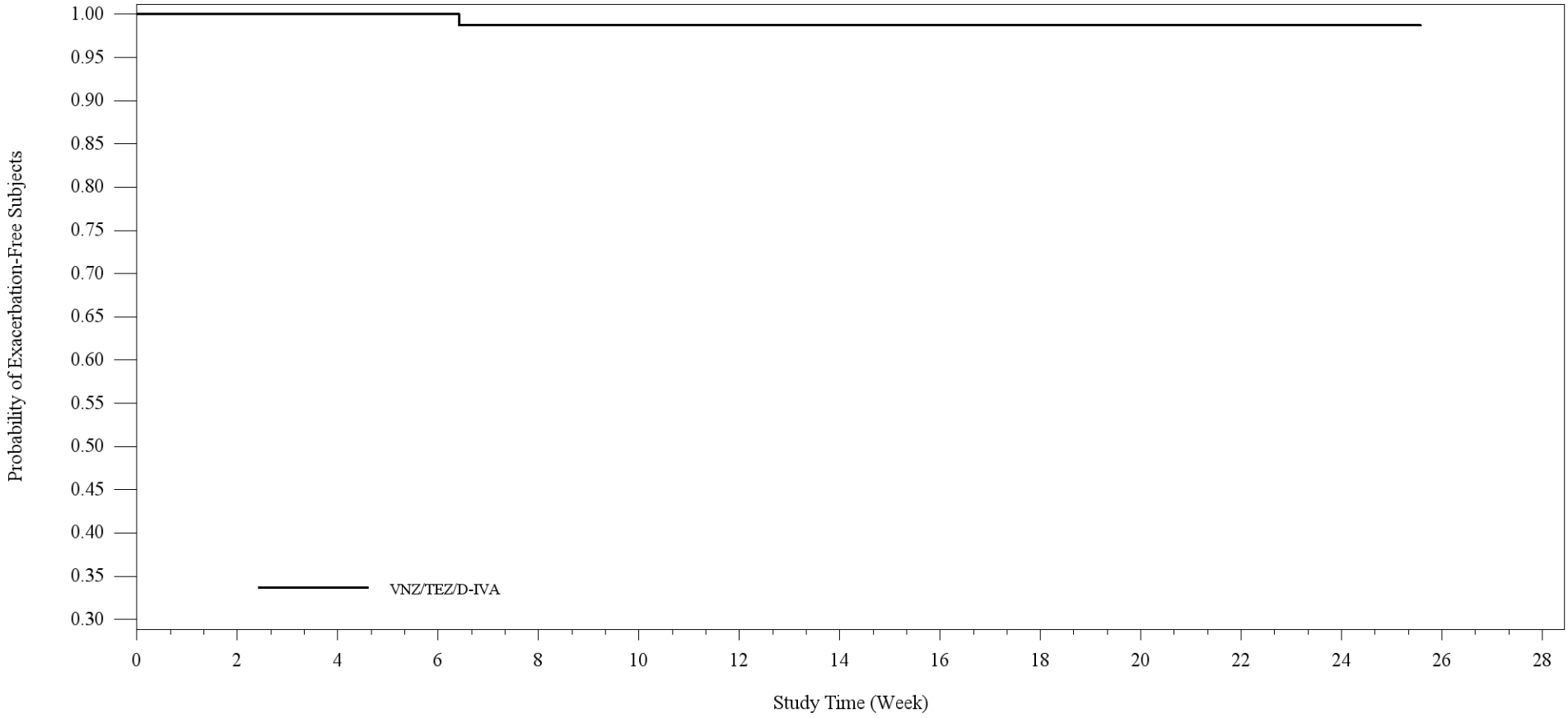


Number of Patients at Risk

VNZ/TEZ/D-IVA	78	78	77	77	77	47

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 3.2.1.16.2
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics through Week 24
Full Analysis Set

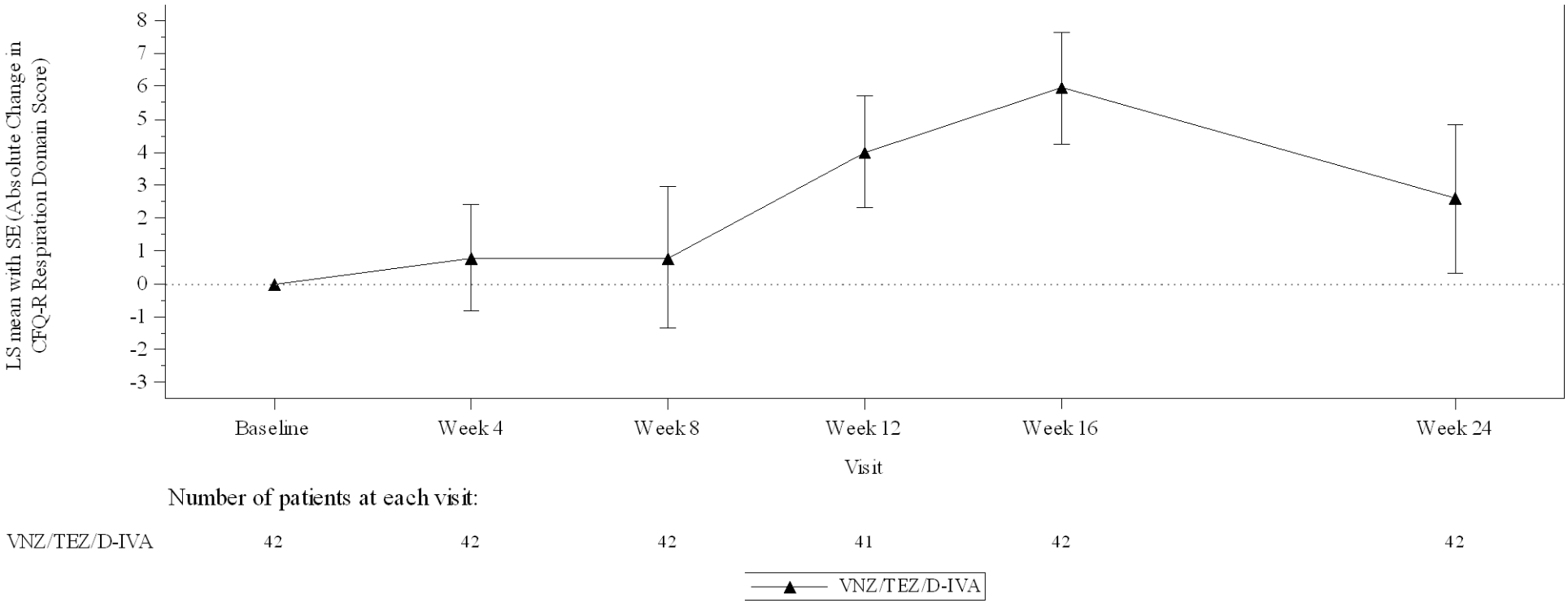


Number of Patients at Risk

VNZ/TEZ/D-IVA	78	78	77	77	77	47

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

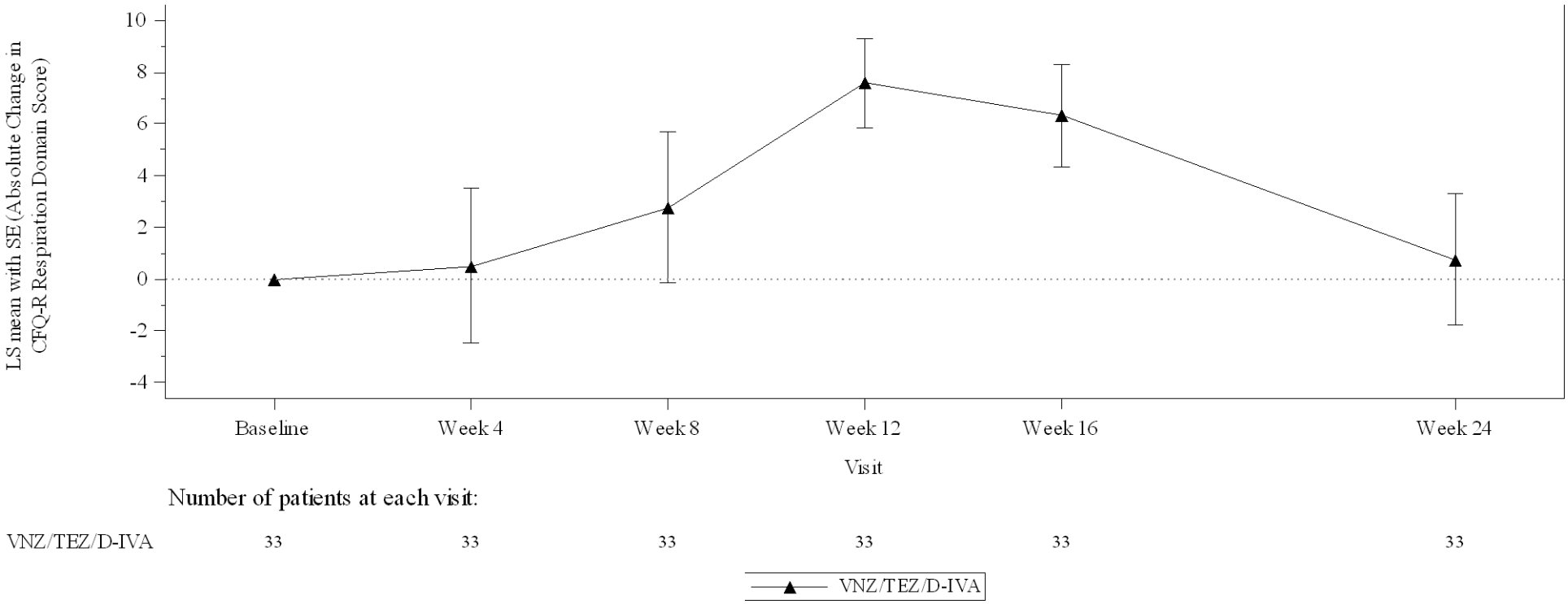
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

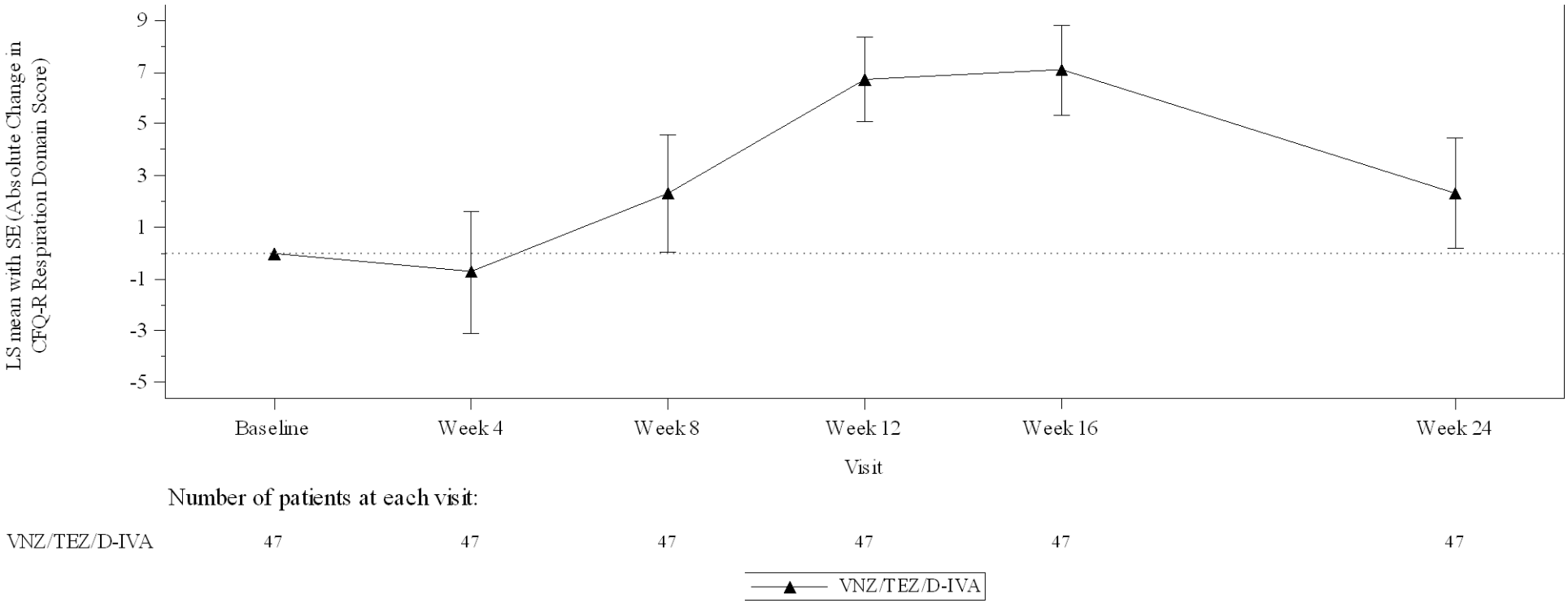
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

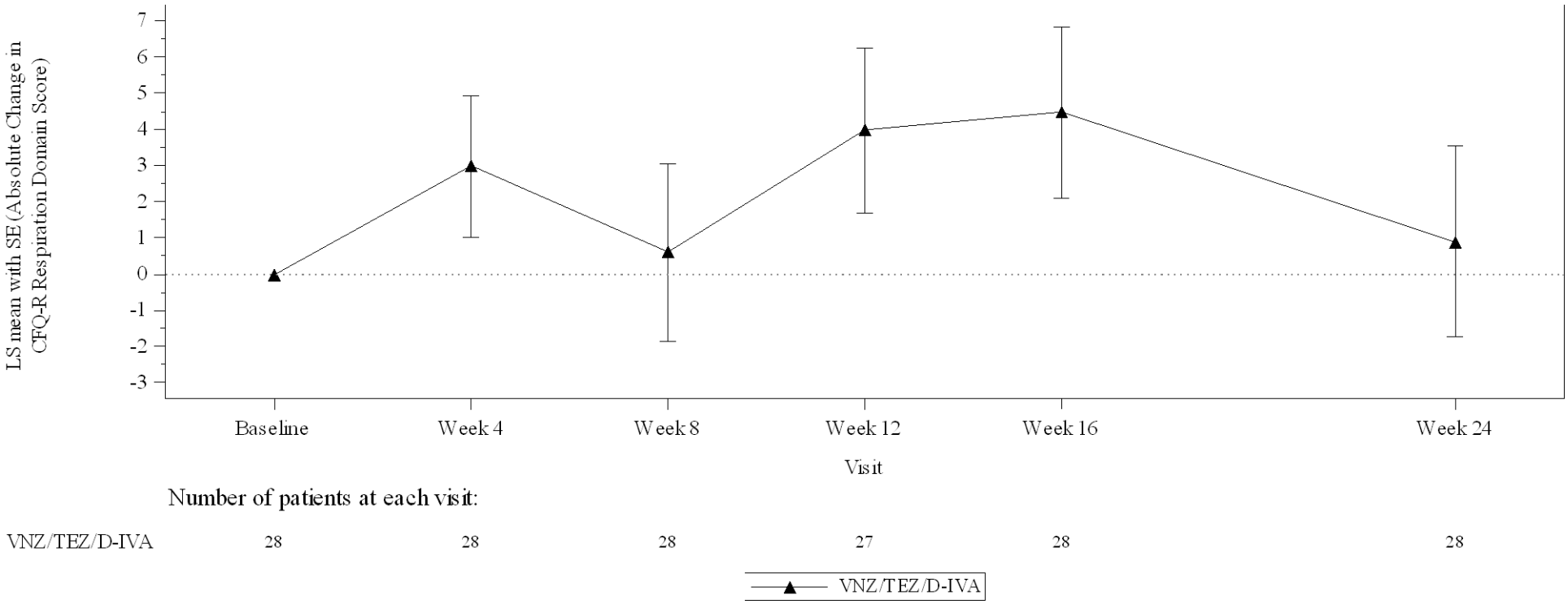
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

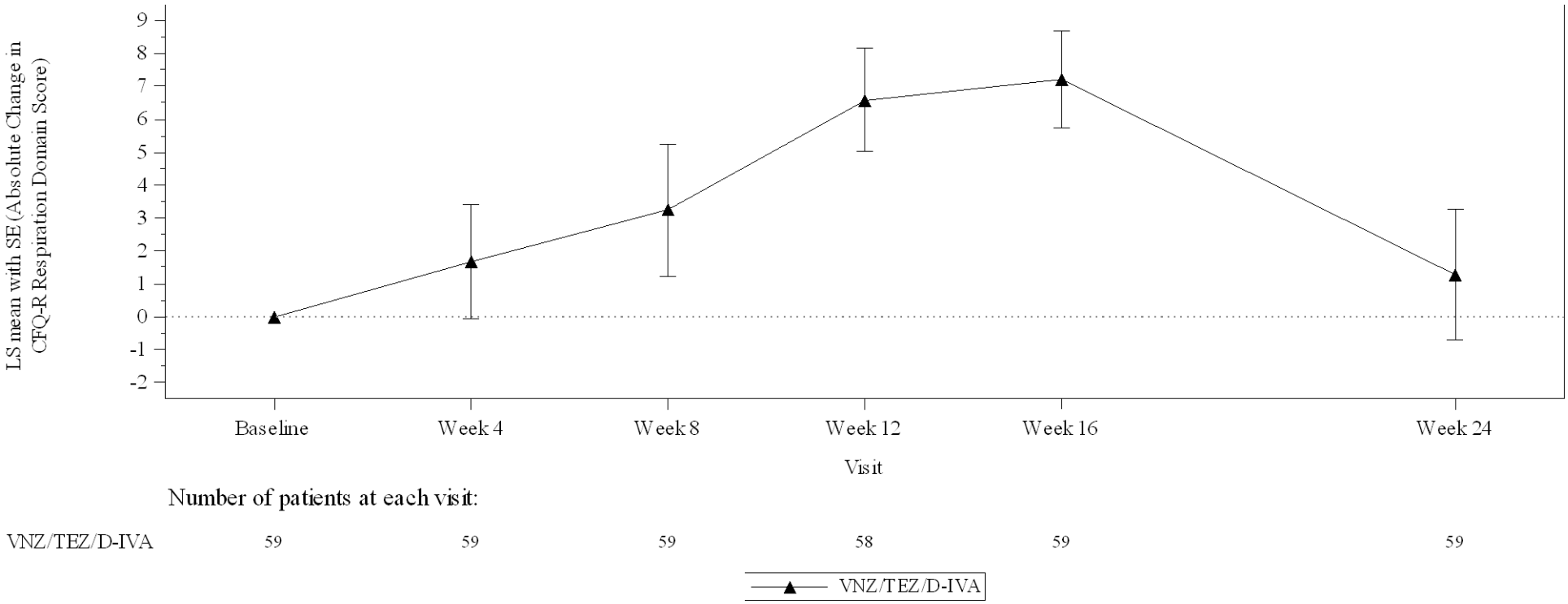
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

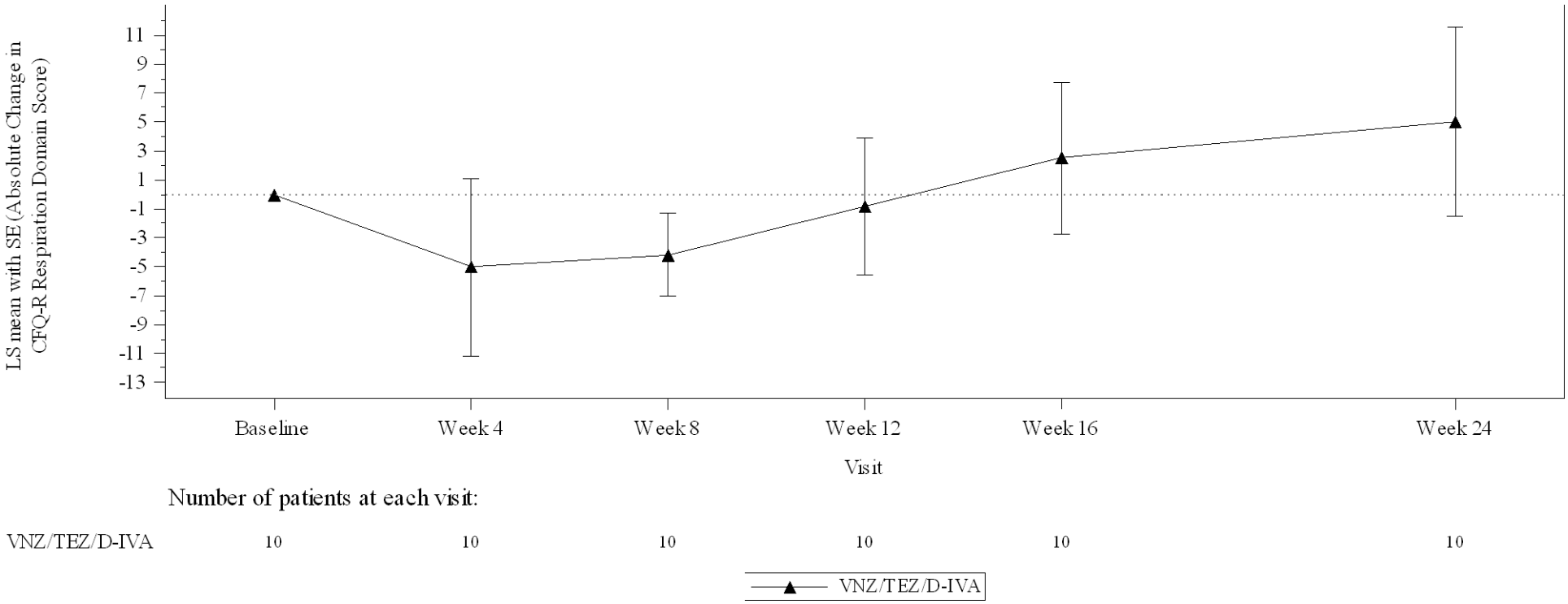
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration
$LCI_{2.5}$ at baseline <7.5



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

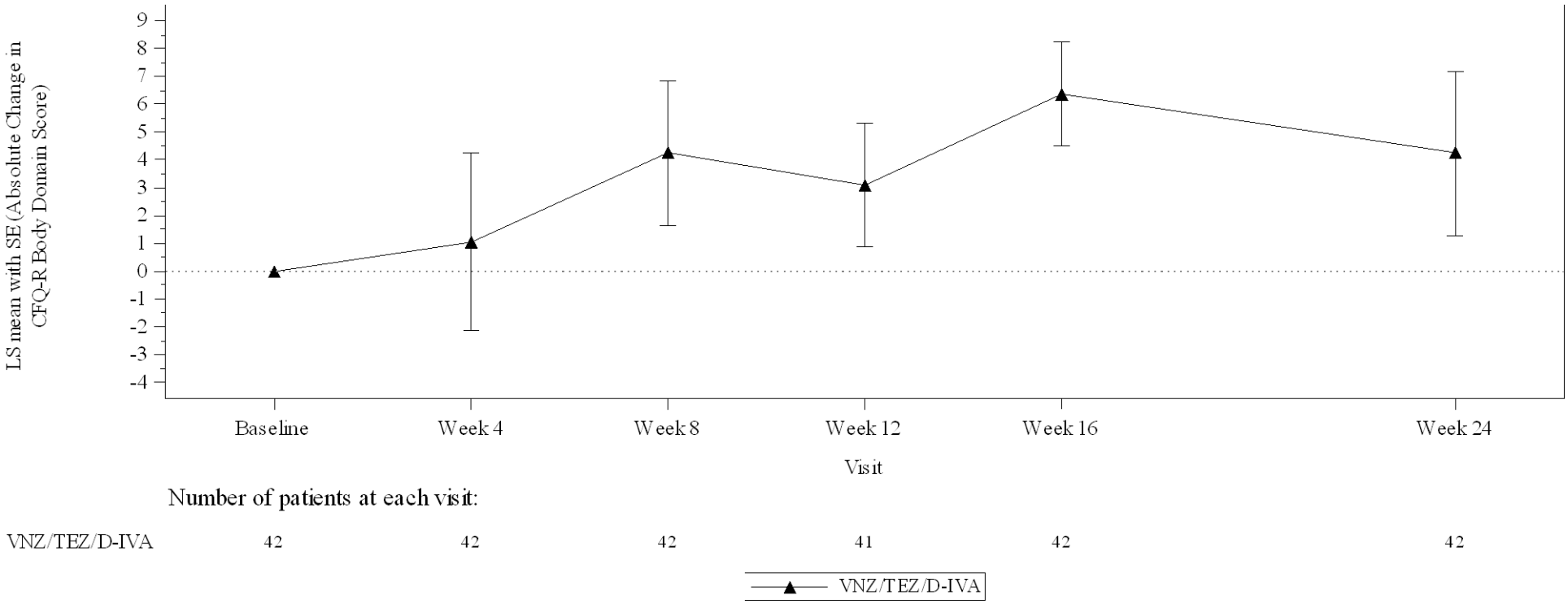
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration
$LCI_{2.5}$ at baseline ≥7.5



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

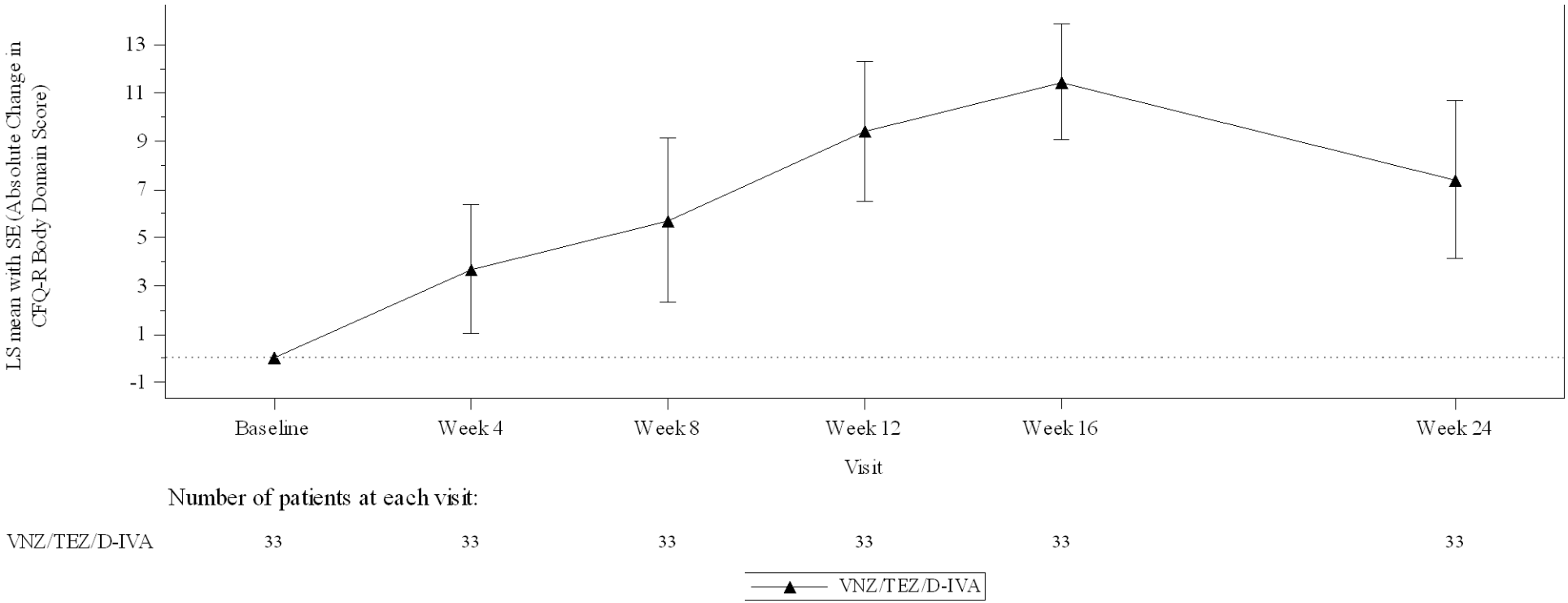
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

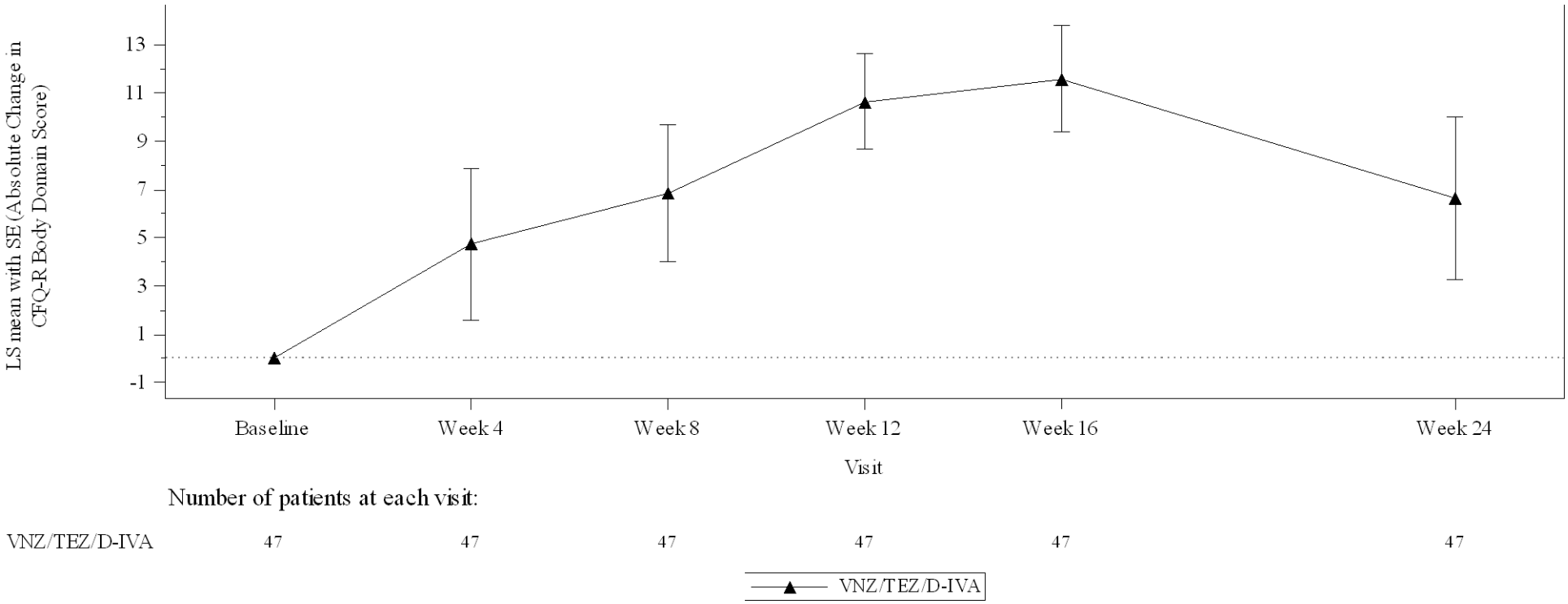
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body
Region = North America



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- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body
Region = Rest of World

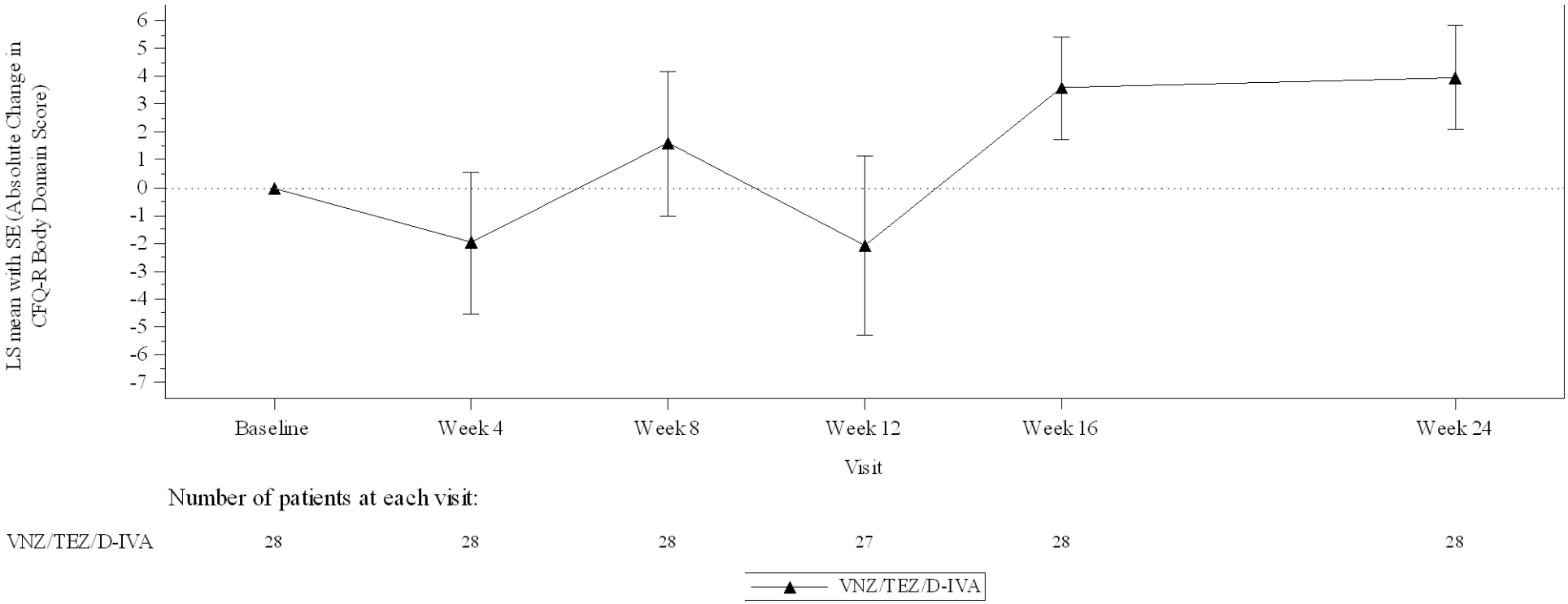

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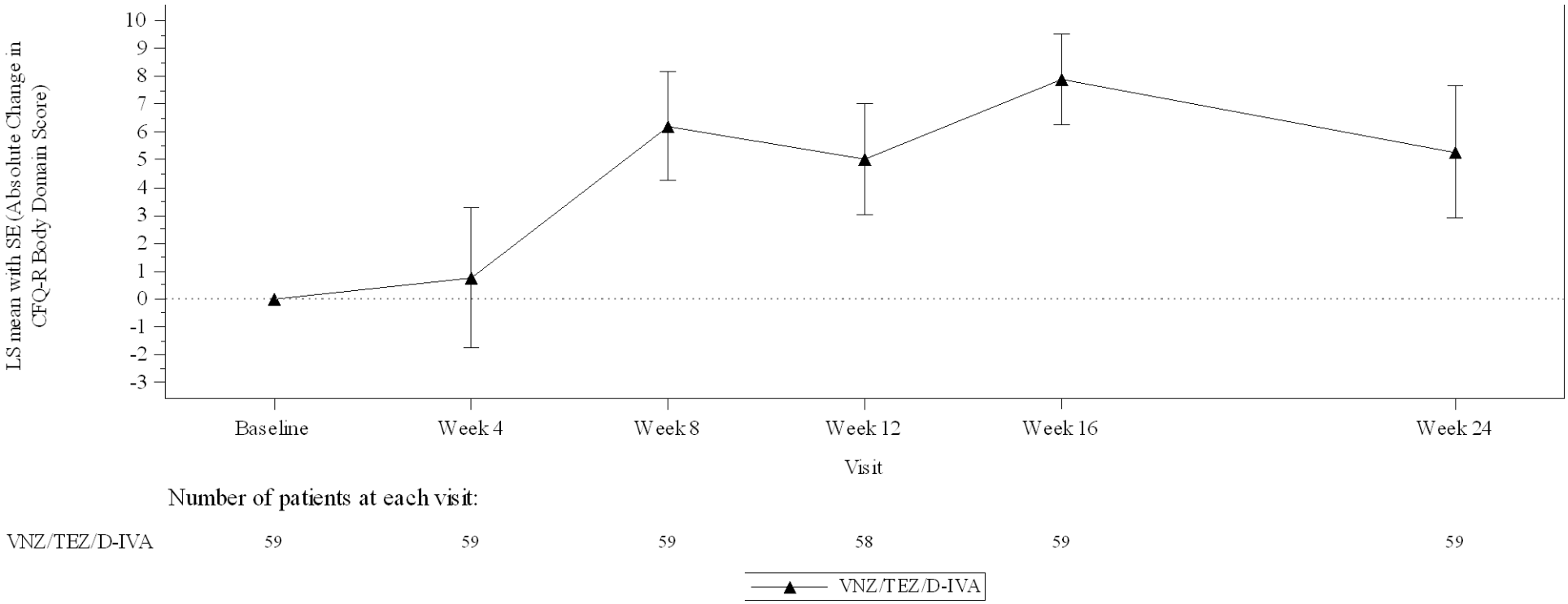
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body
$LCI_{2.5}$ at baseline <7.5



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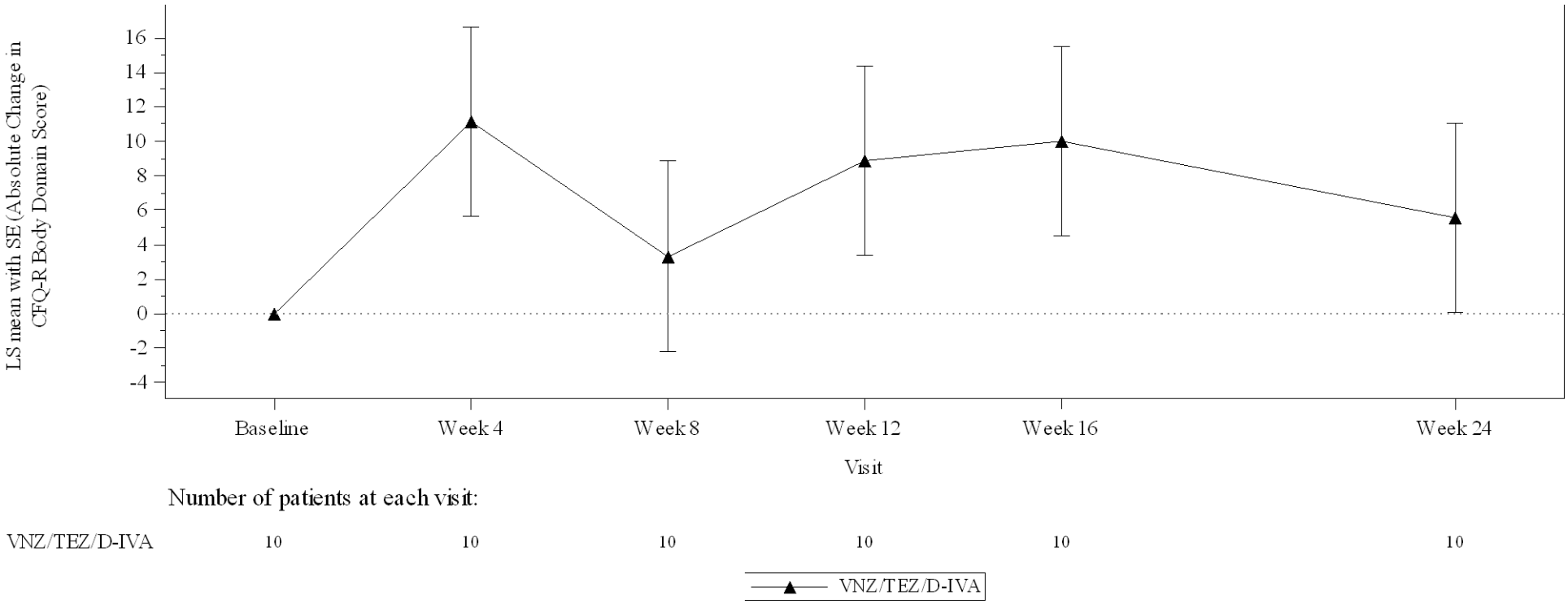
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body
$LCI_{2.5}$ at baseline ≥7.5



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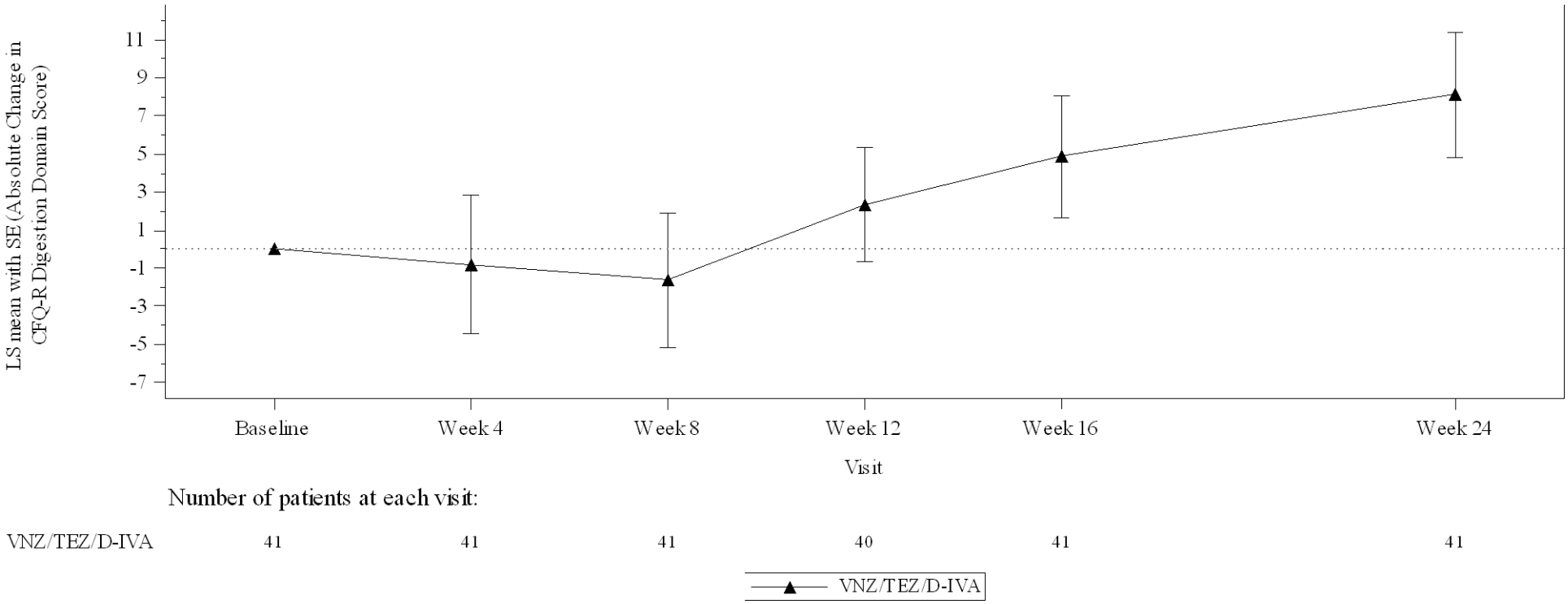
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion
Sex = Male



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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion
Sex = Female

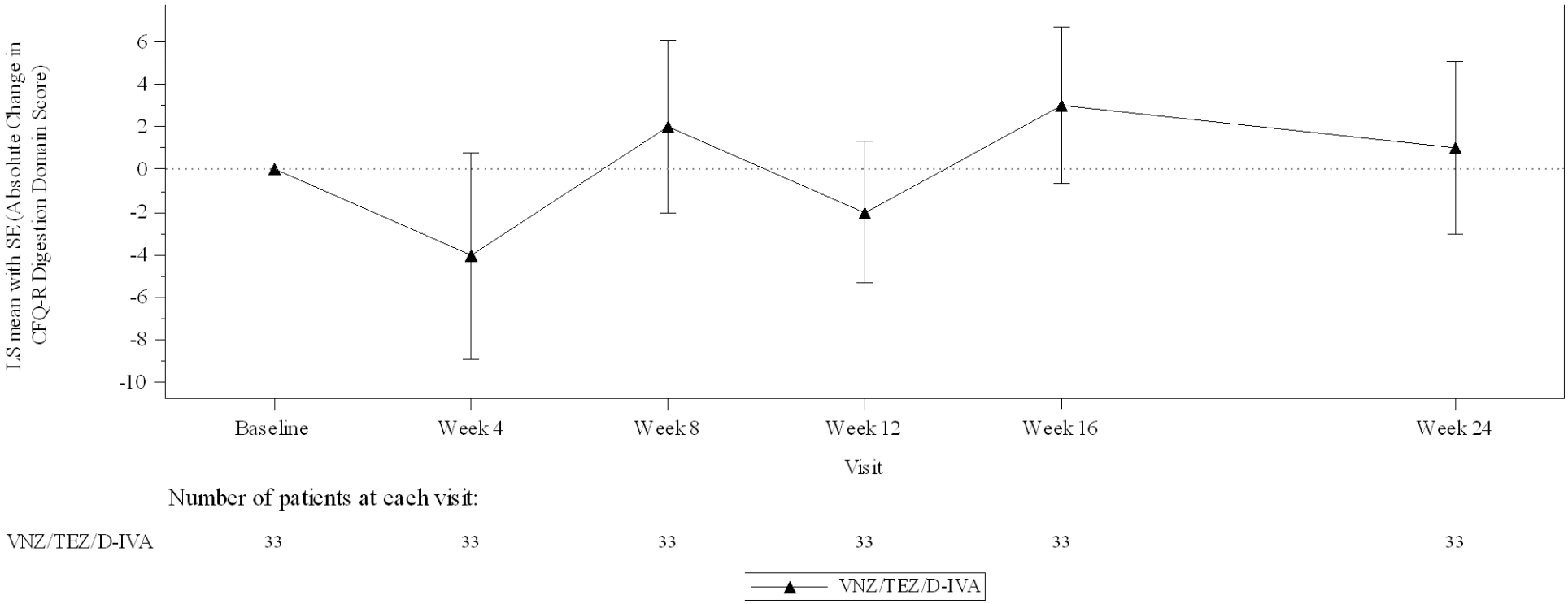

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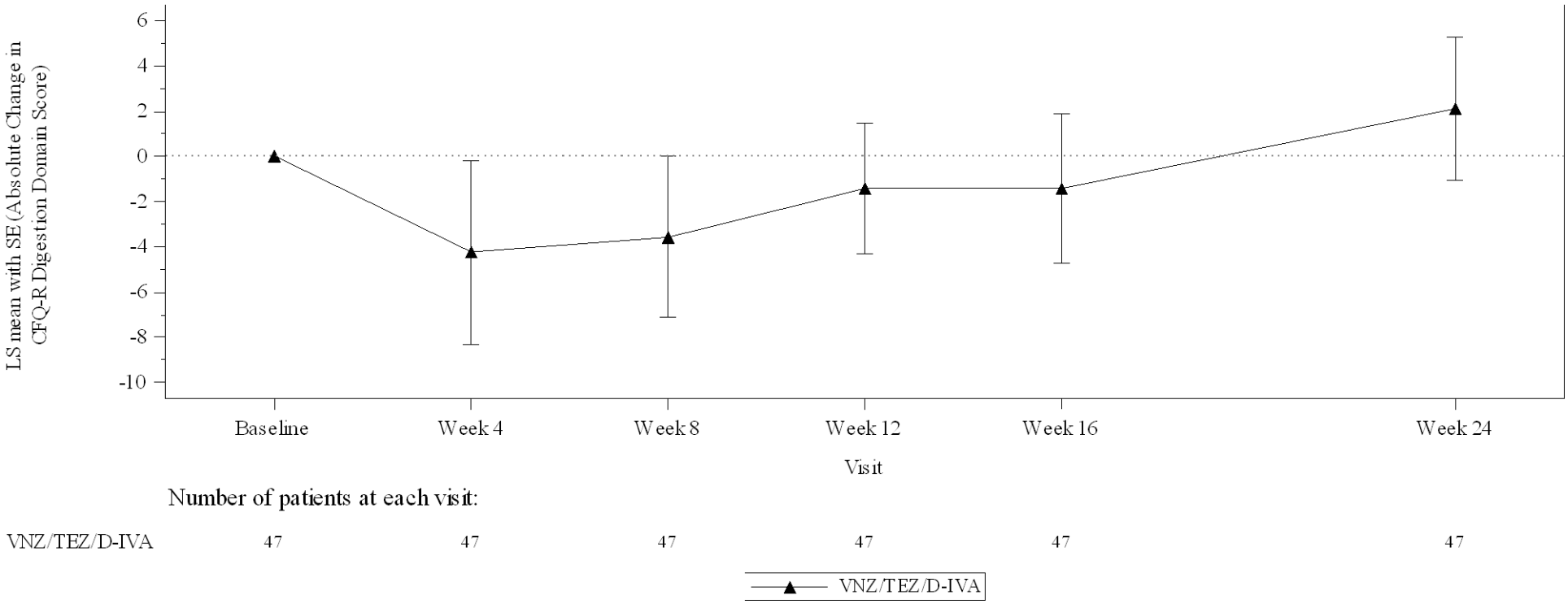
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion
Region = North America



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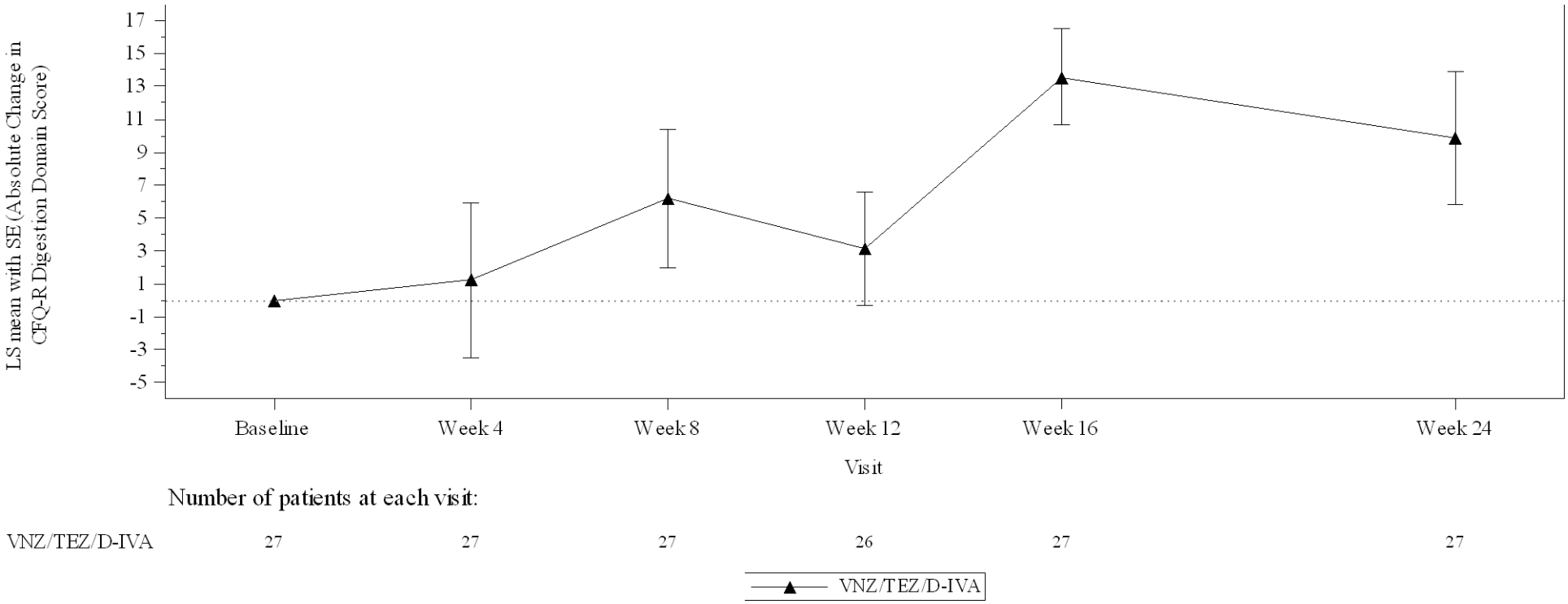
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion
Region = Rest of World



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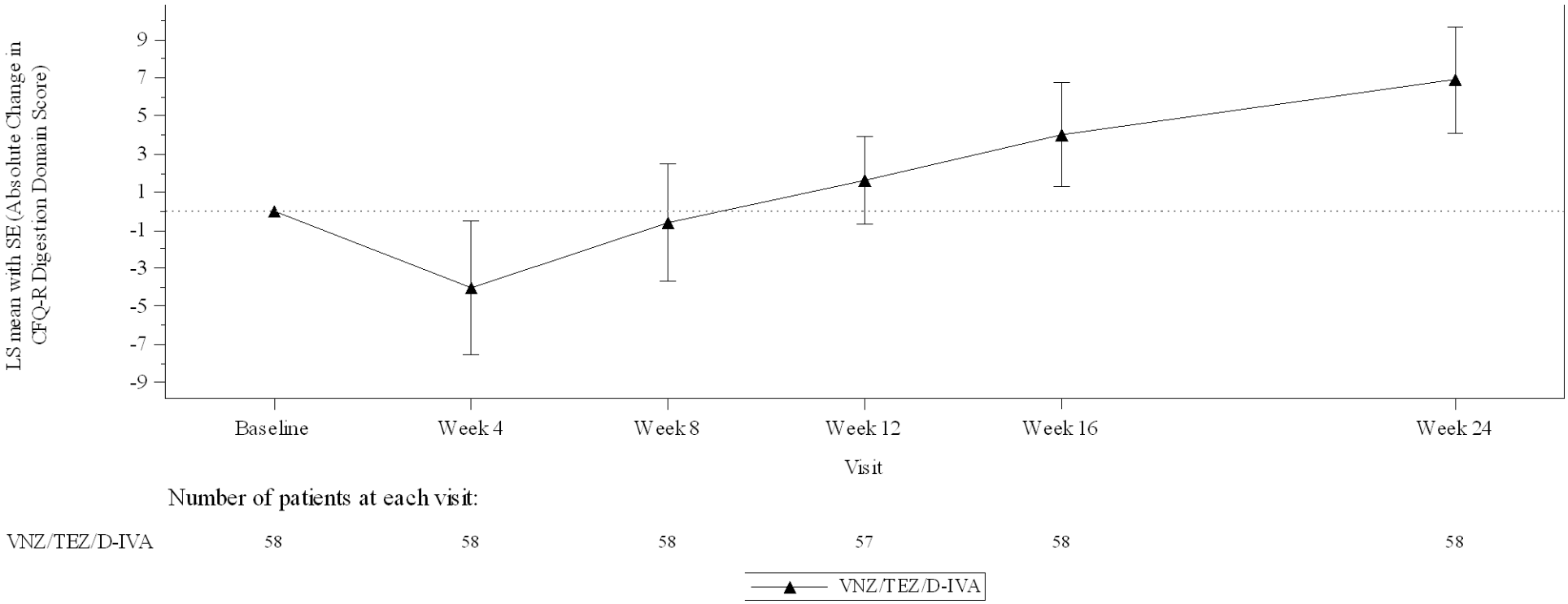
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion
$LCI_{2.5}$ at baseline <7.5



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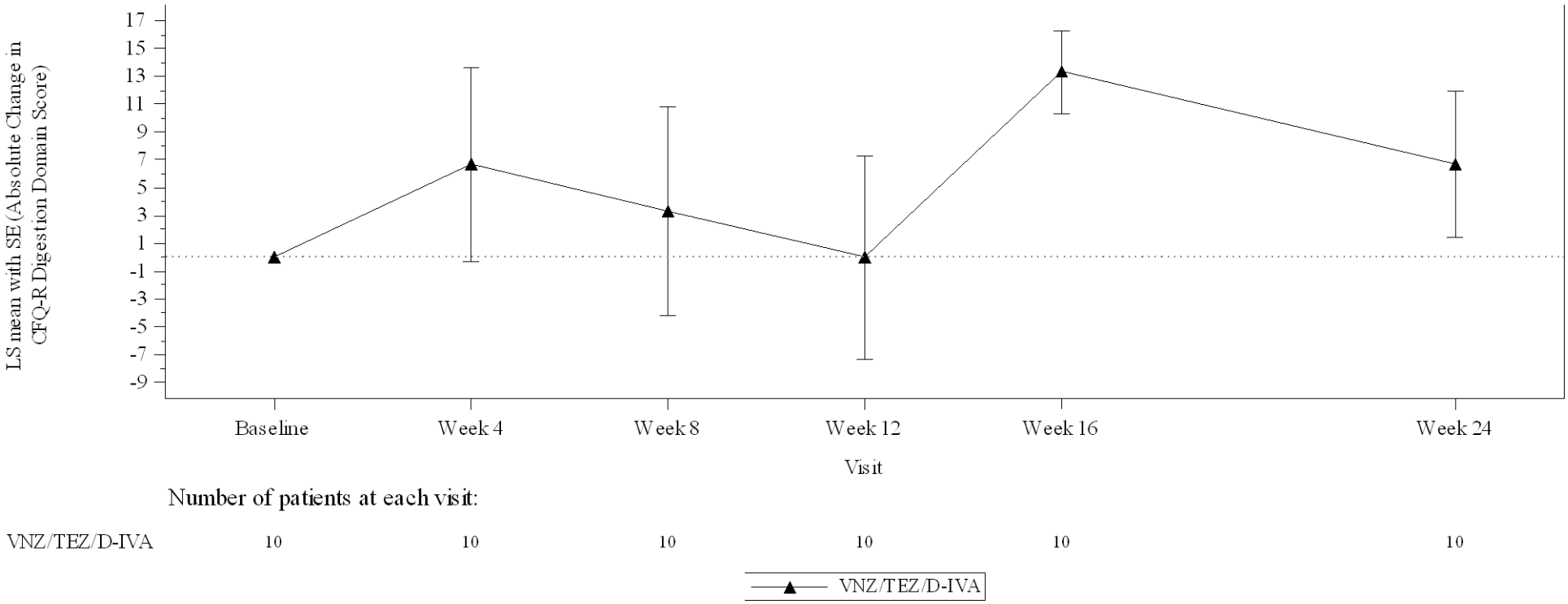
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion
$LCI_{2.5}$ at baseline ≥7.5



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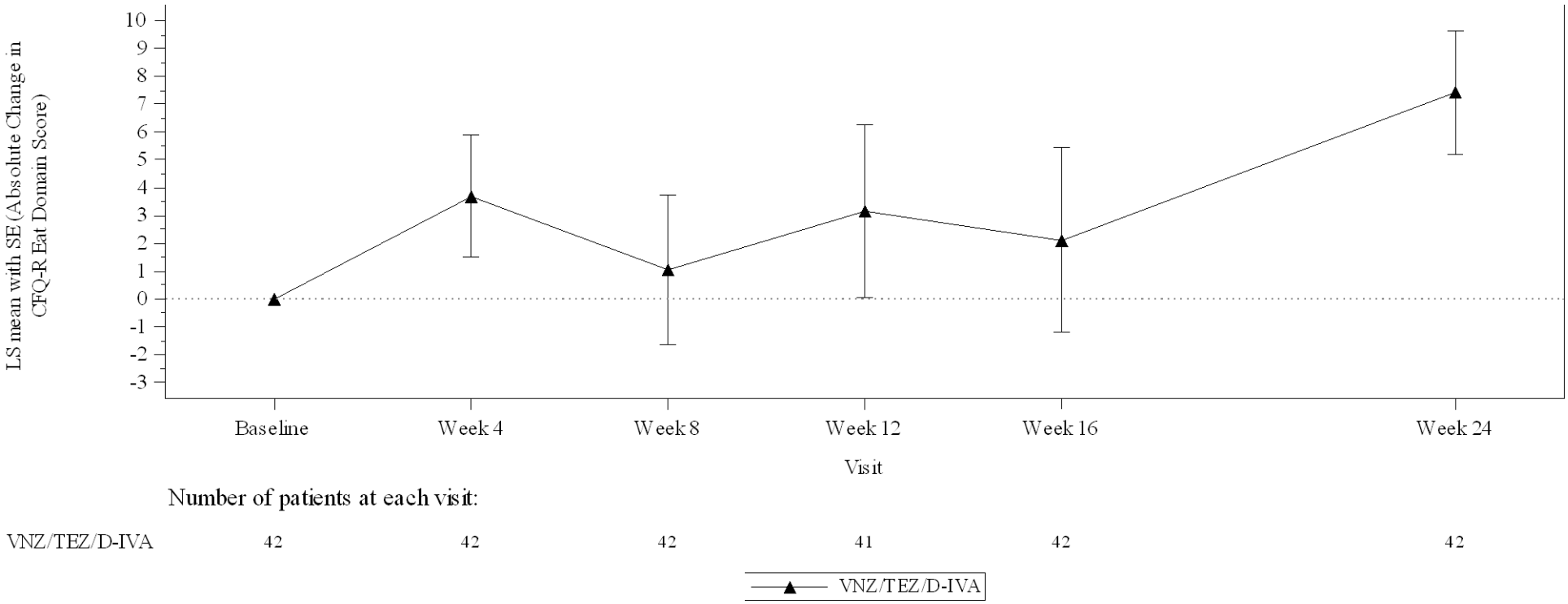
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat
Sex = Male



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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat
Sex = Female

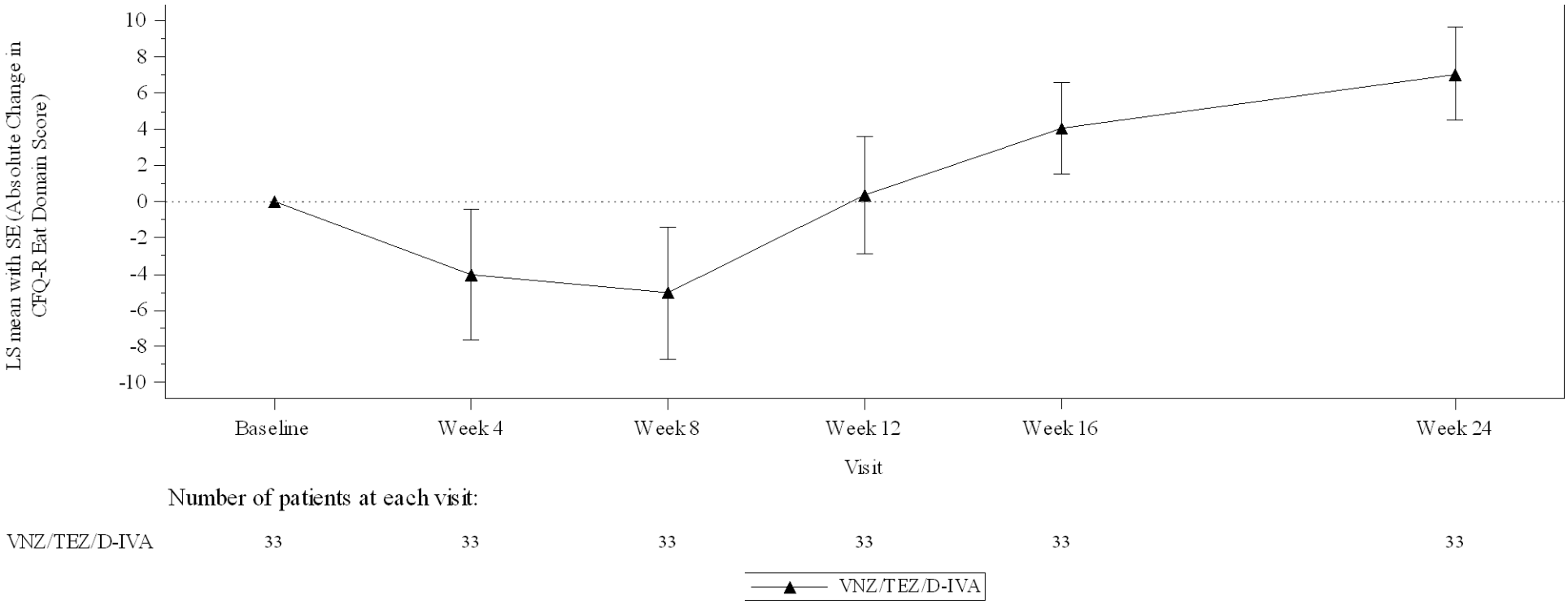

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Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat
Region = North America

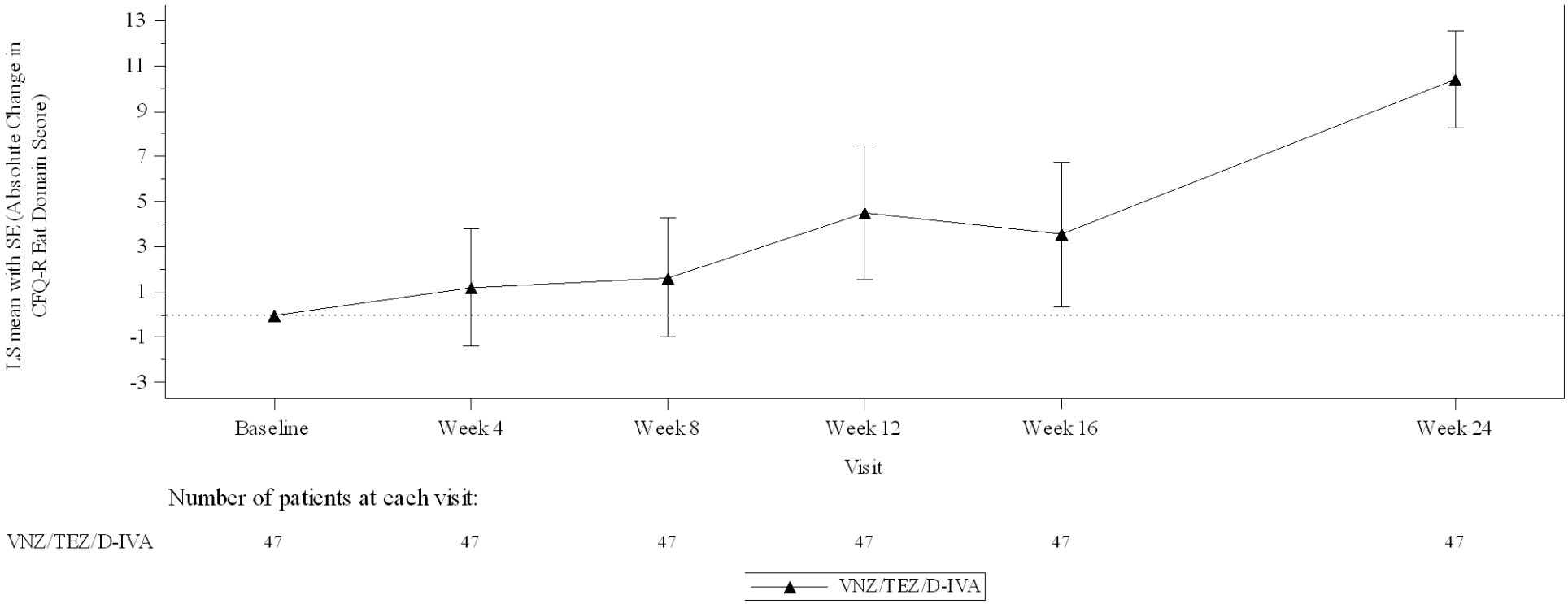

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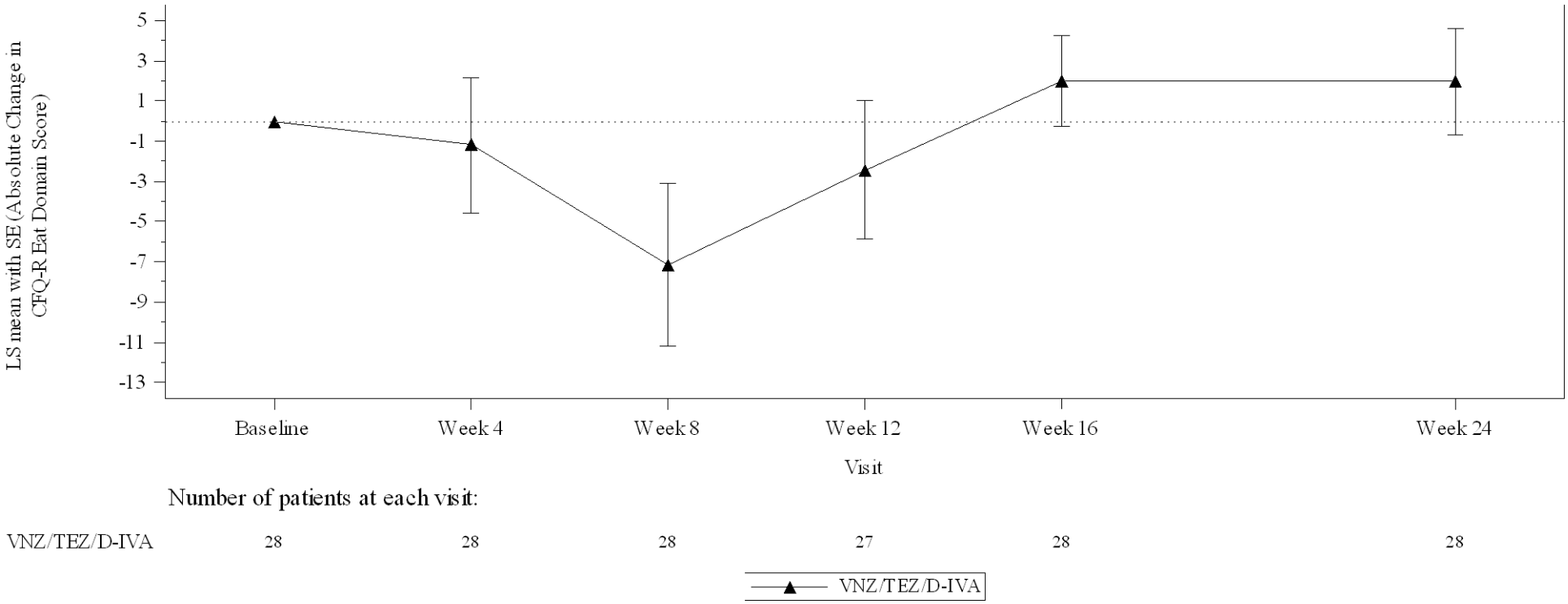
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat
Region = Rest of World



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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat
$LCI_{2.5}$ at baseline <7.5

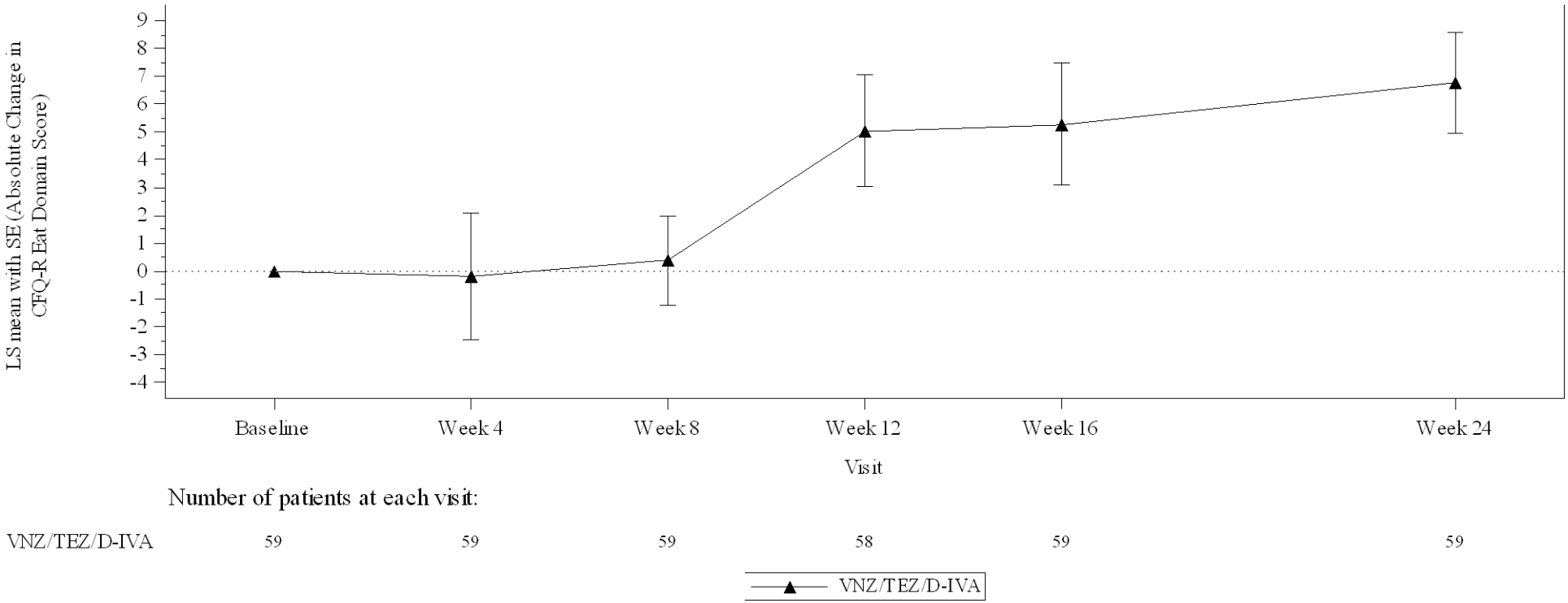

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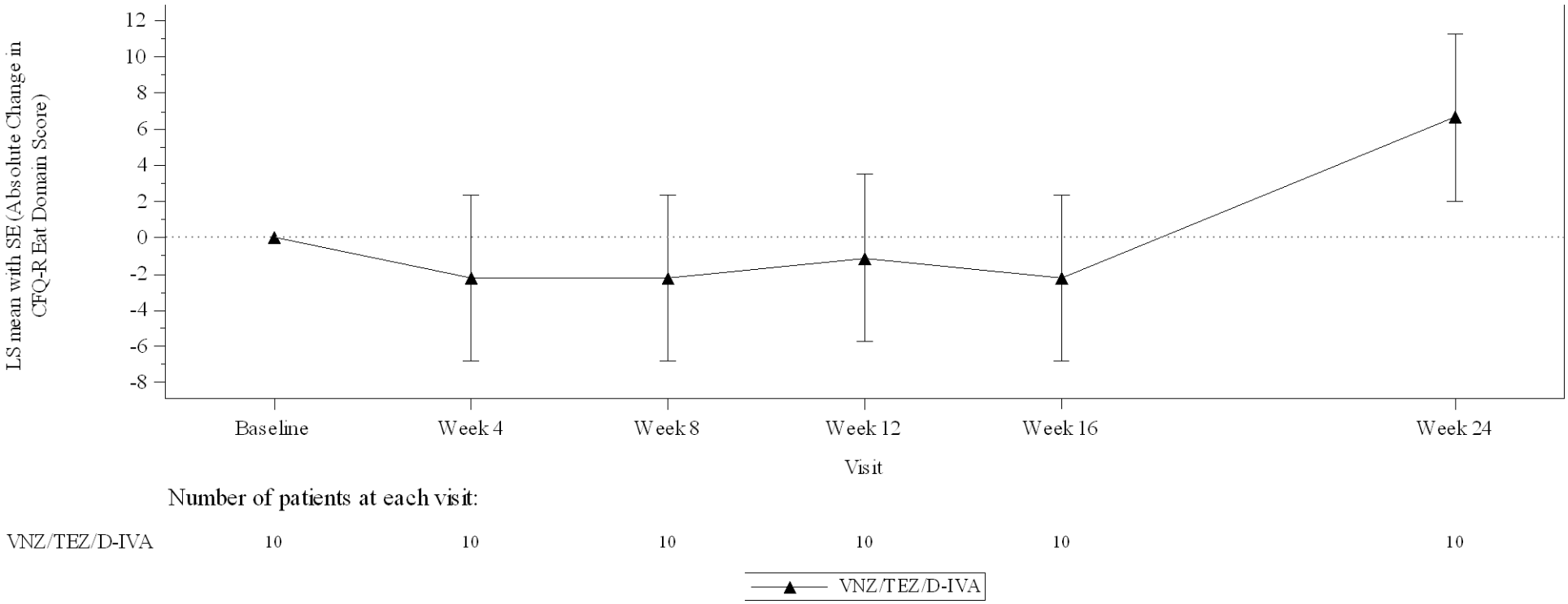
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat
$LCI_{2.5}$ at baseline ≥7.5



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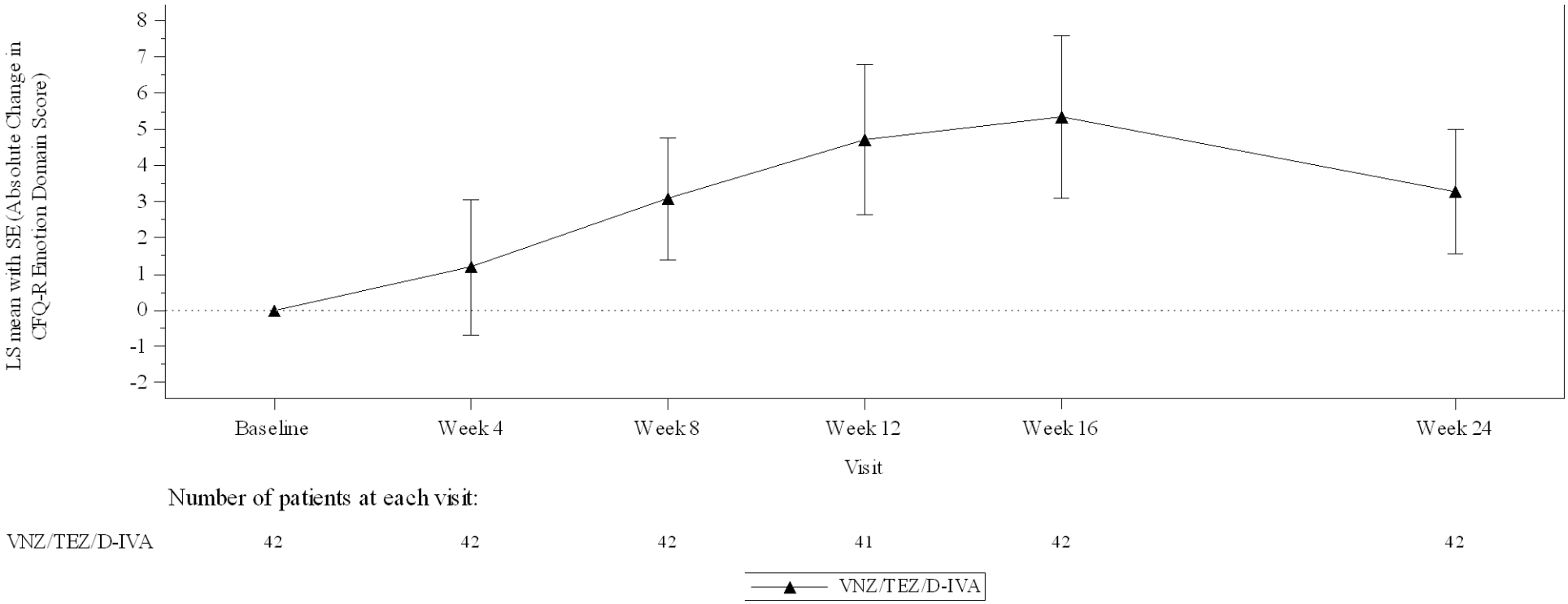
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion
Sex = Male



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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion
Sex = Female

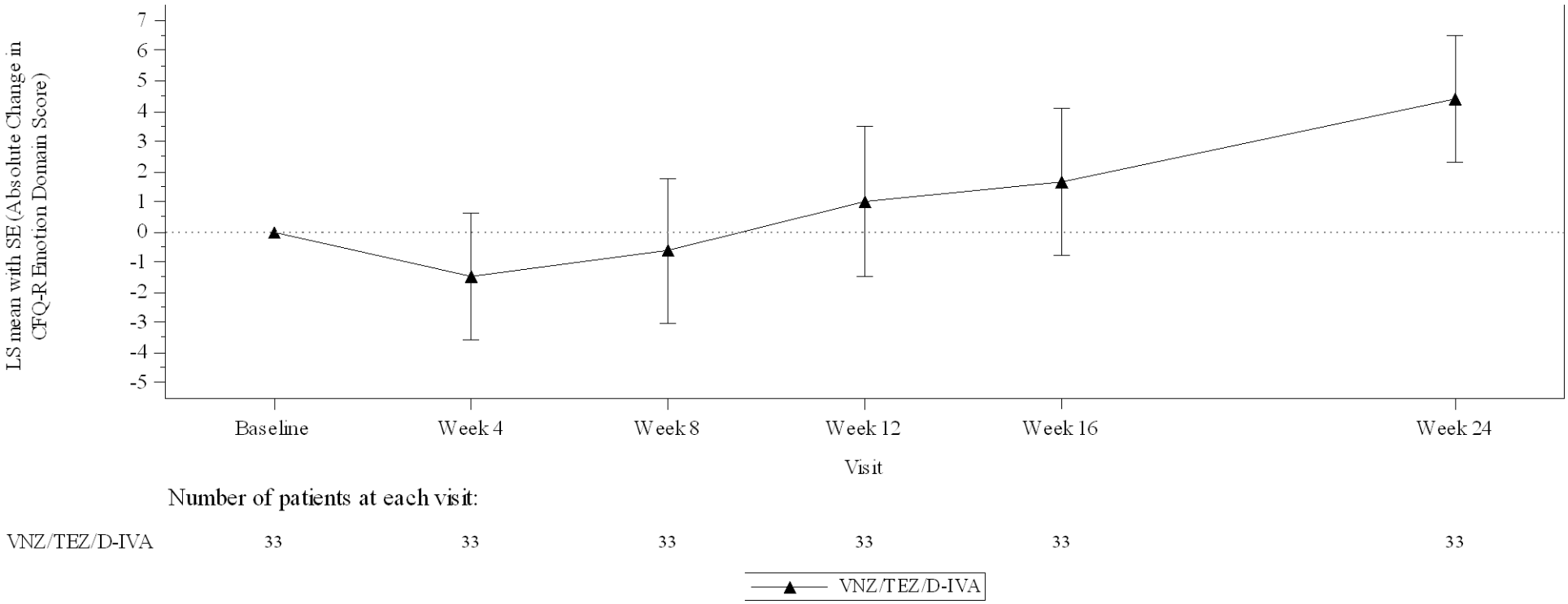

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Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion
Region = North America

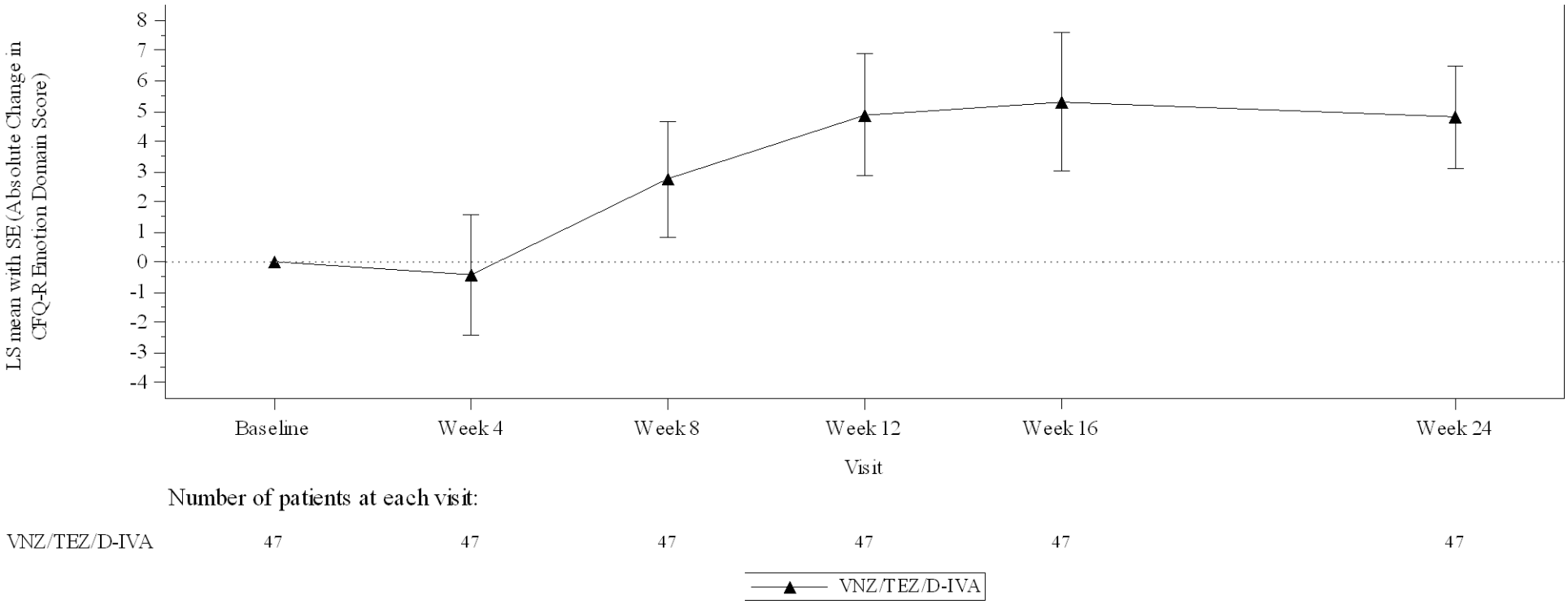

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Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion
Region = Rest of World

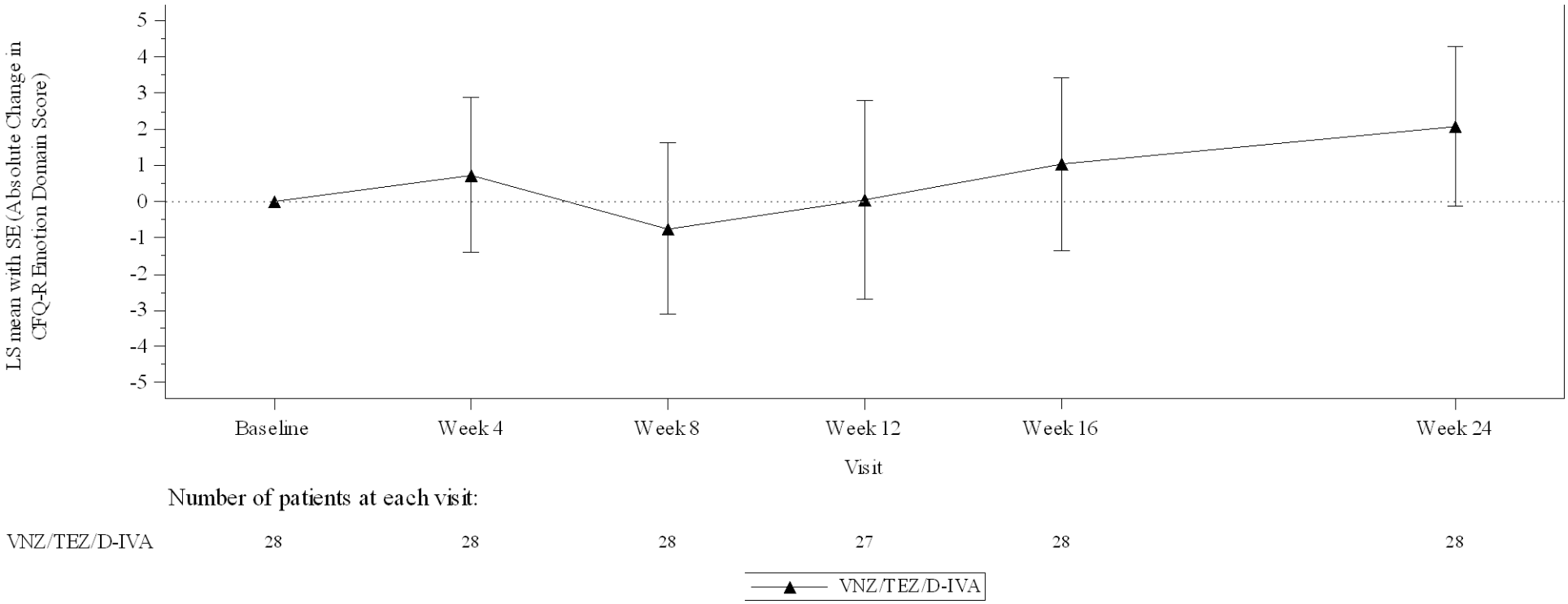

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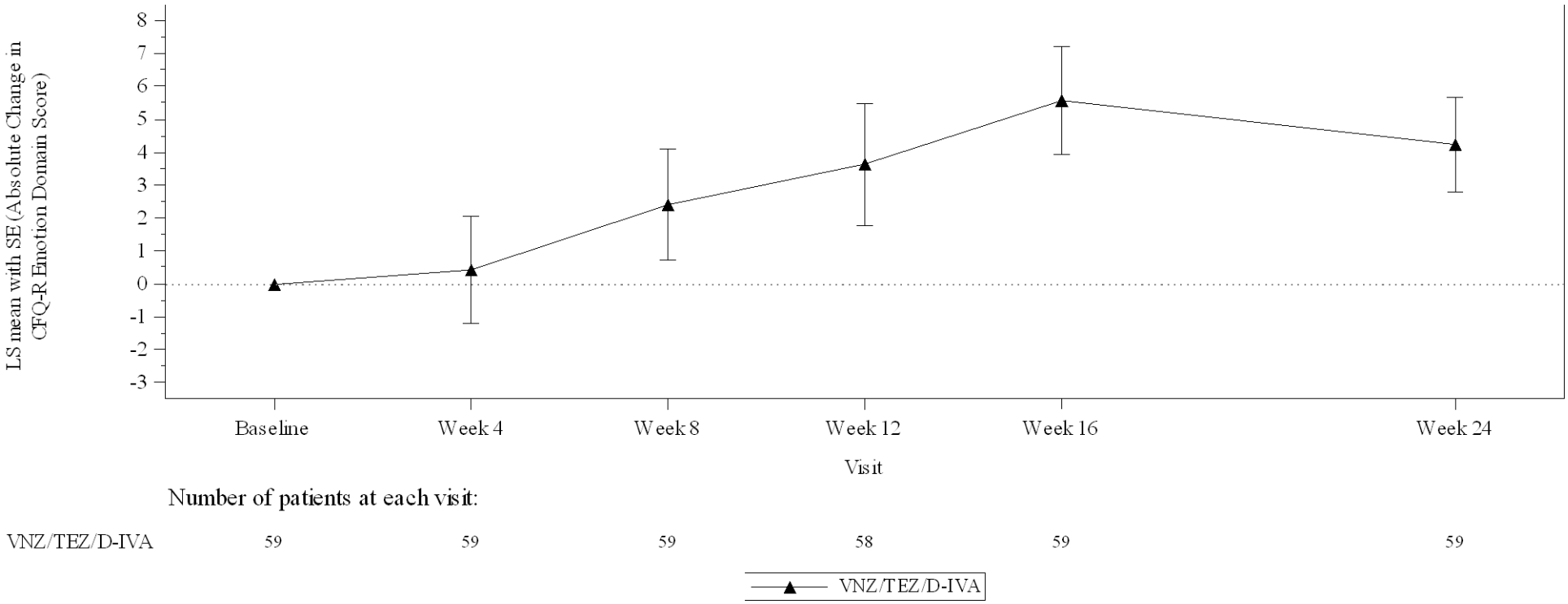
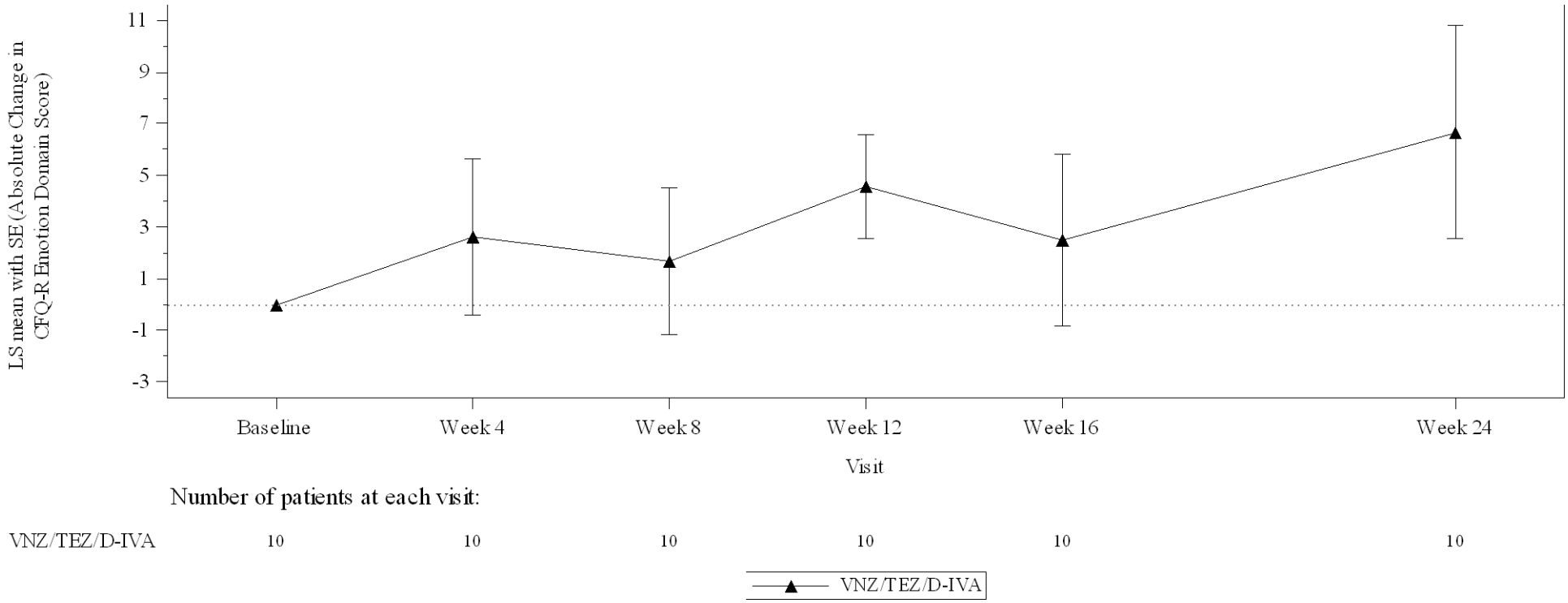
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion
$LCI_{2.5}$ at baseline <7.5



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

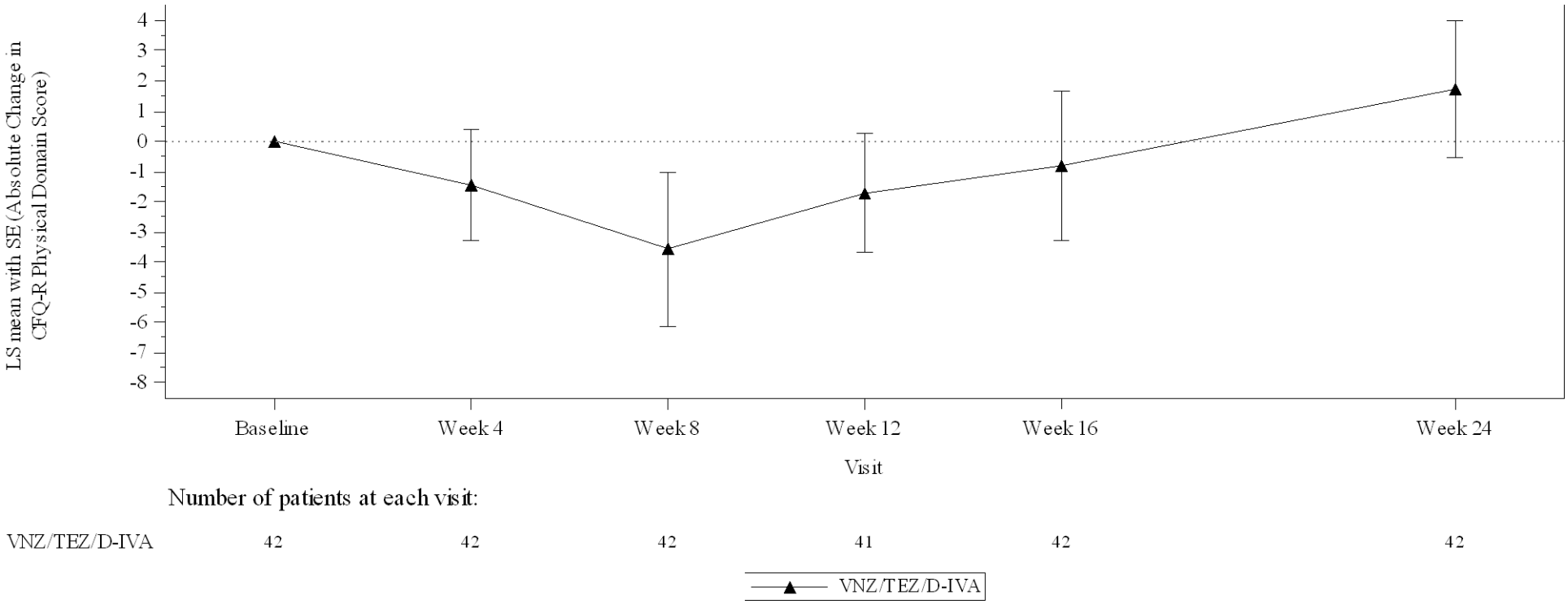
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion
$LCI_{2.5}$ at baseline ≥7.5



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

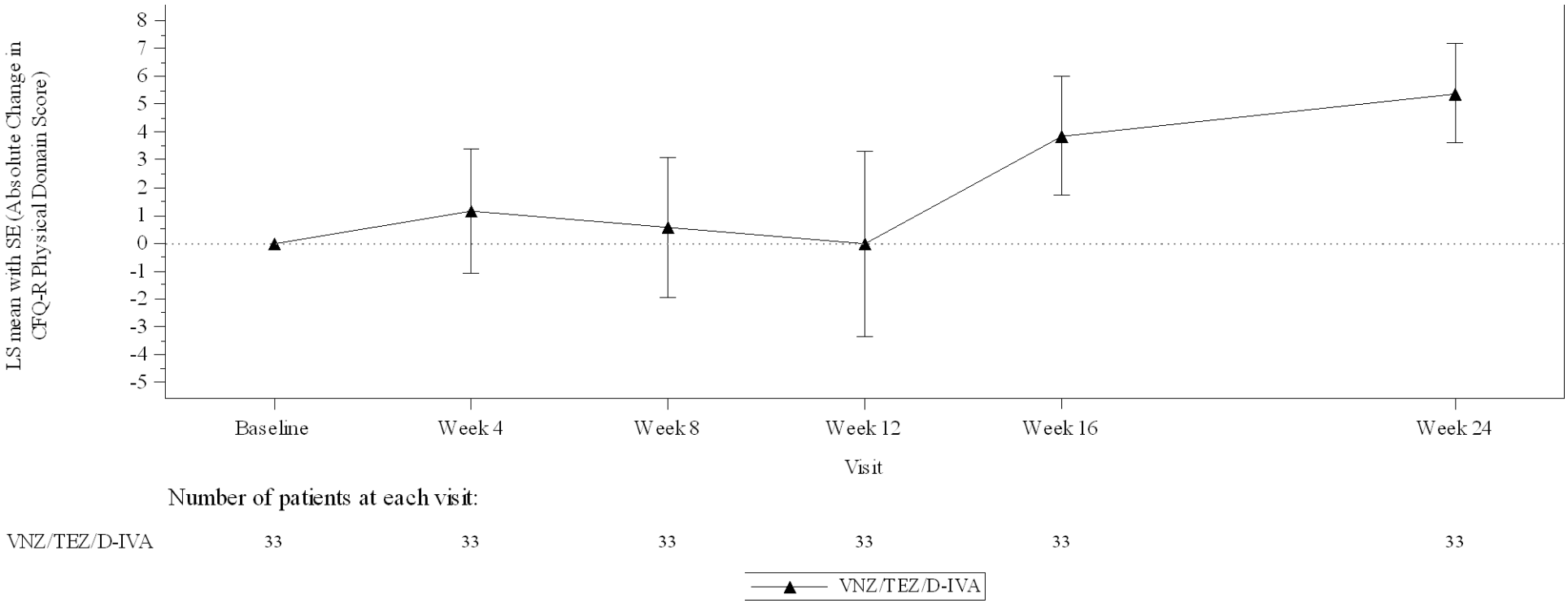
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

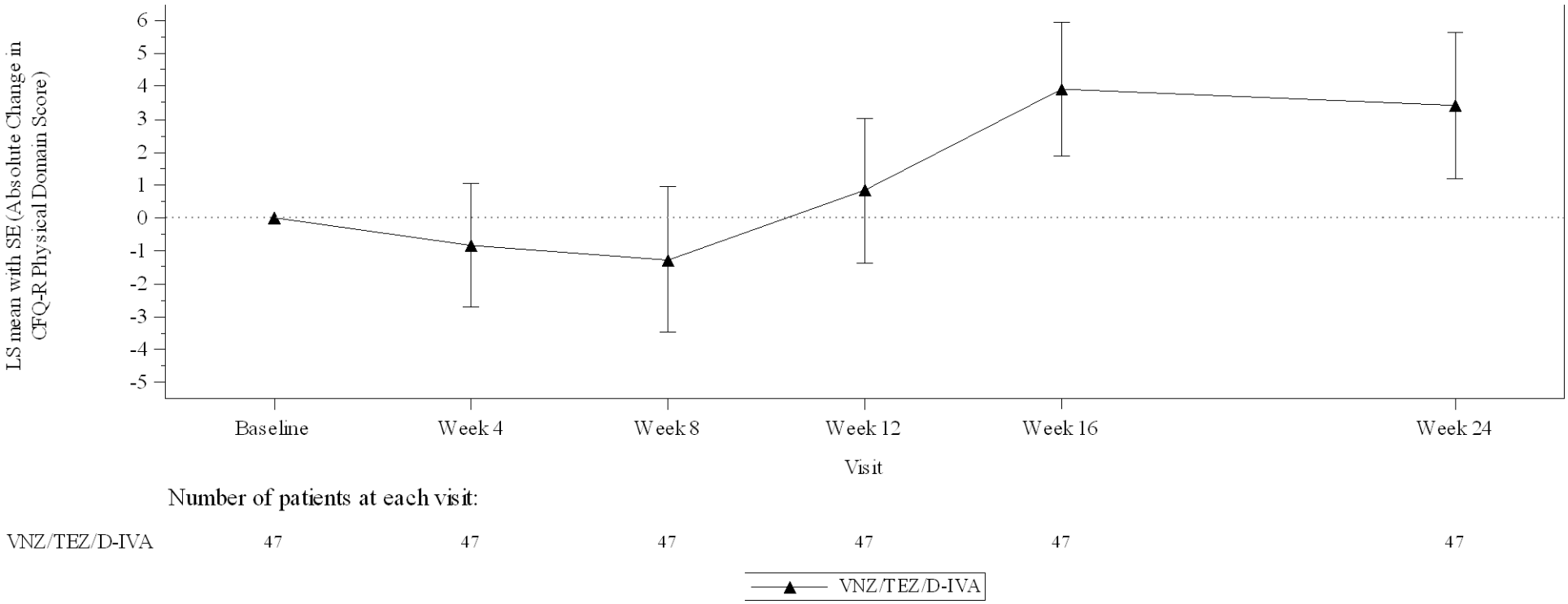
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

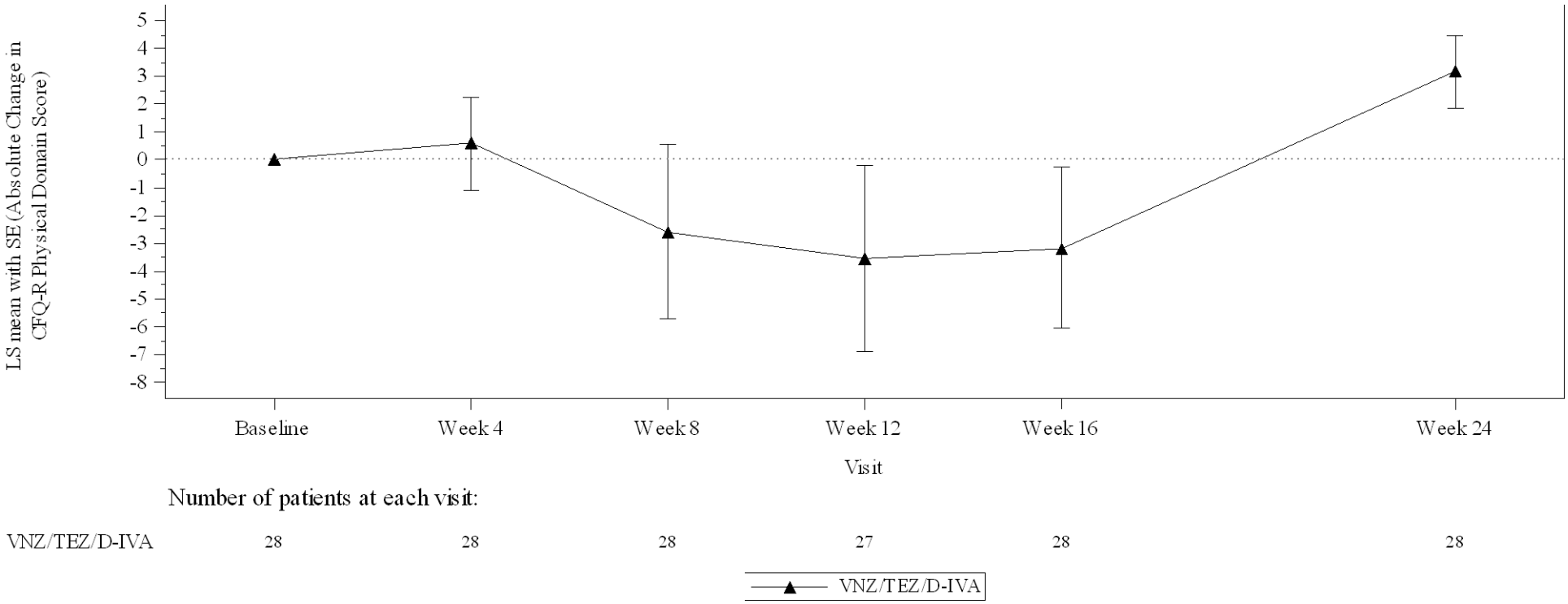
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

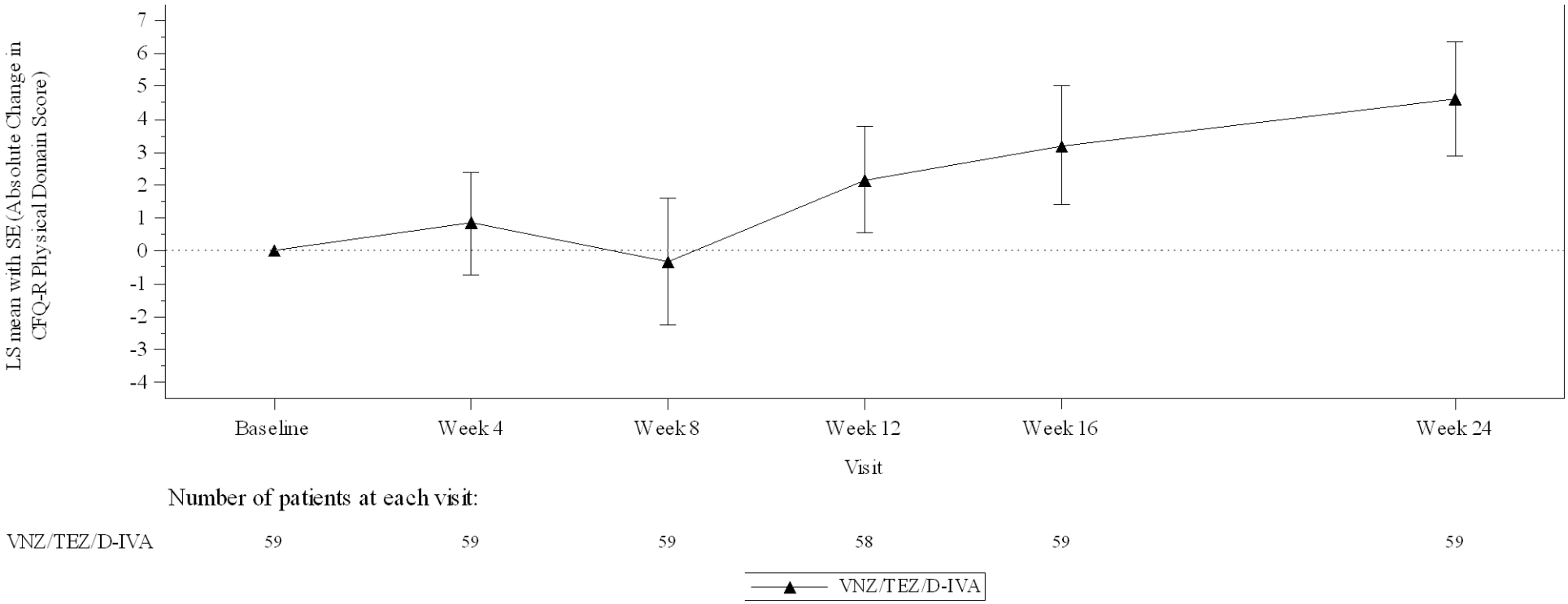
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

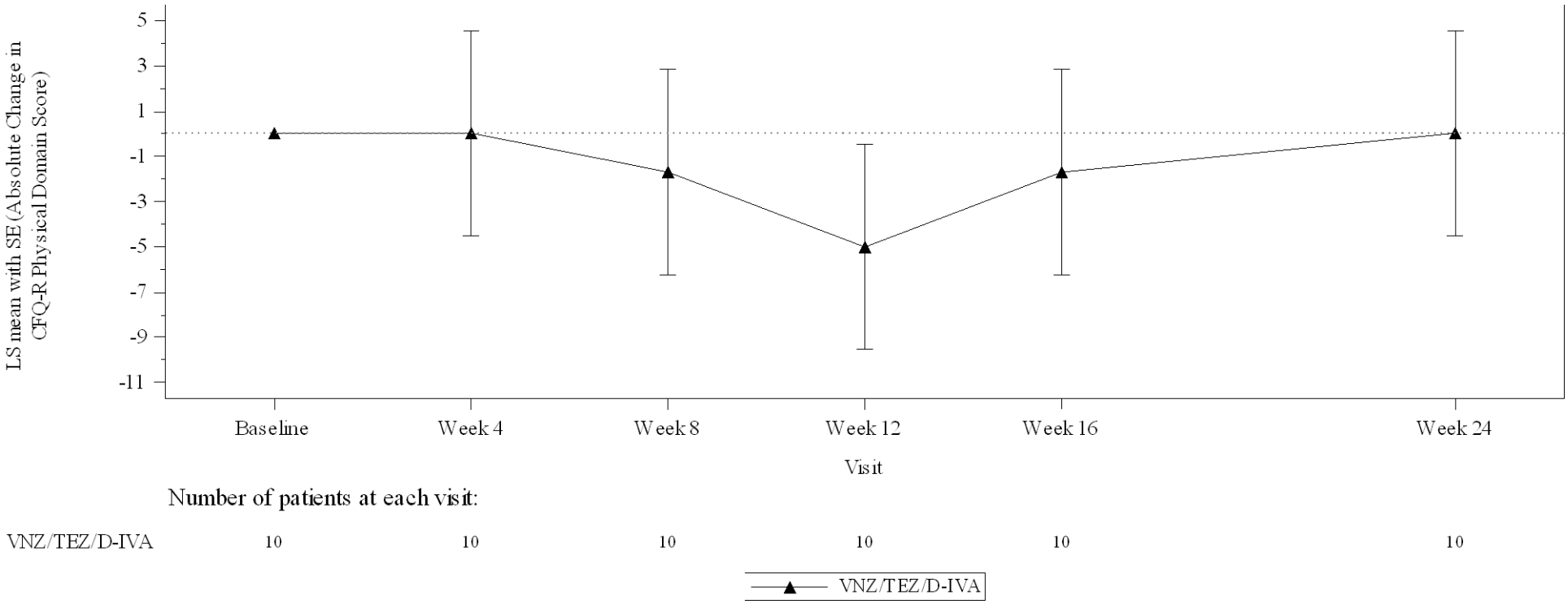
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical
$LCI_{2.5}$ at baseline <7.5



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

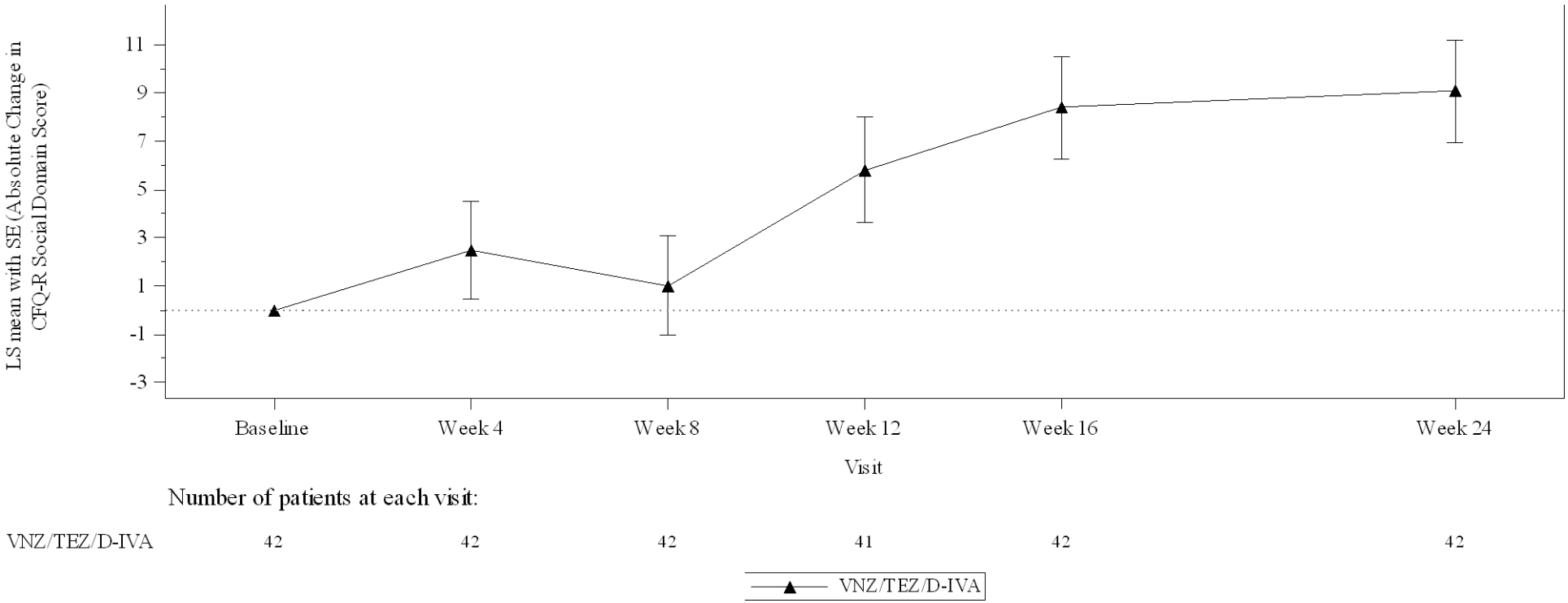
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical
$LCI_{2.5}$ at baseline ≥7.5



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

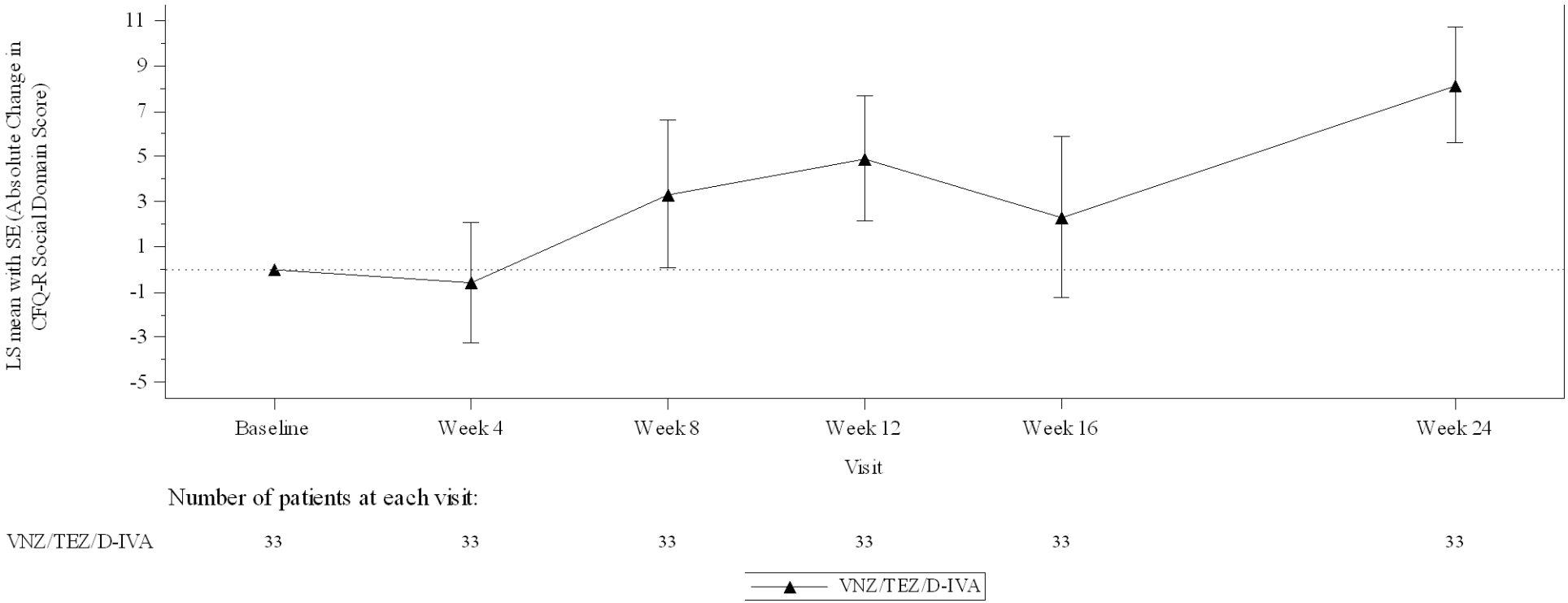
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Social
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

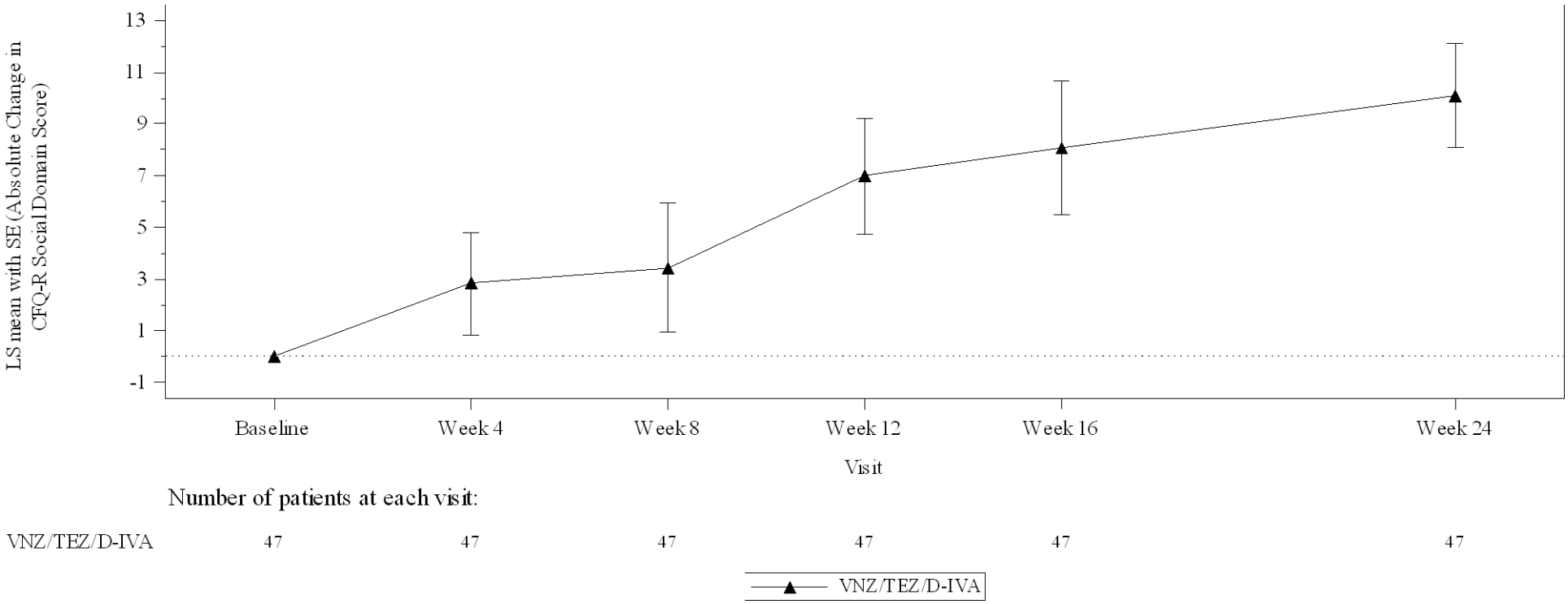
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Social
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

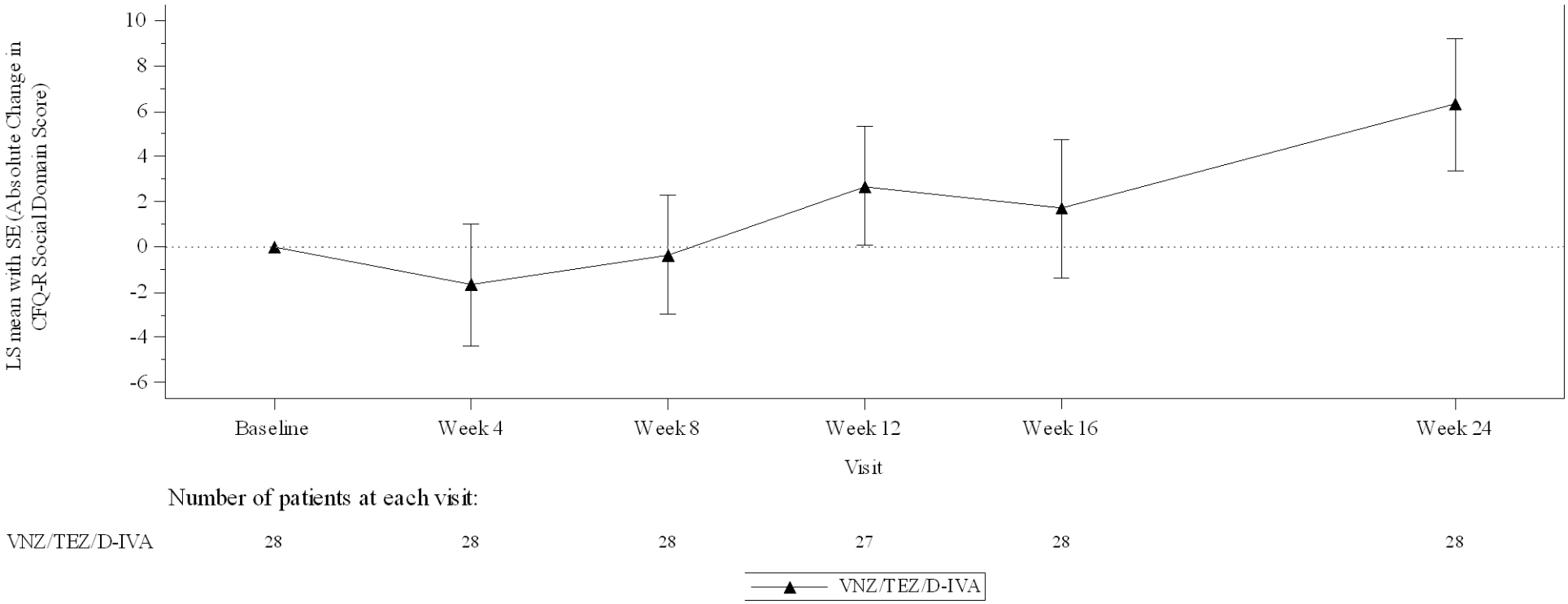
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Social
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

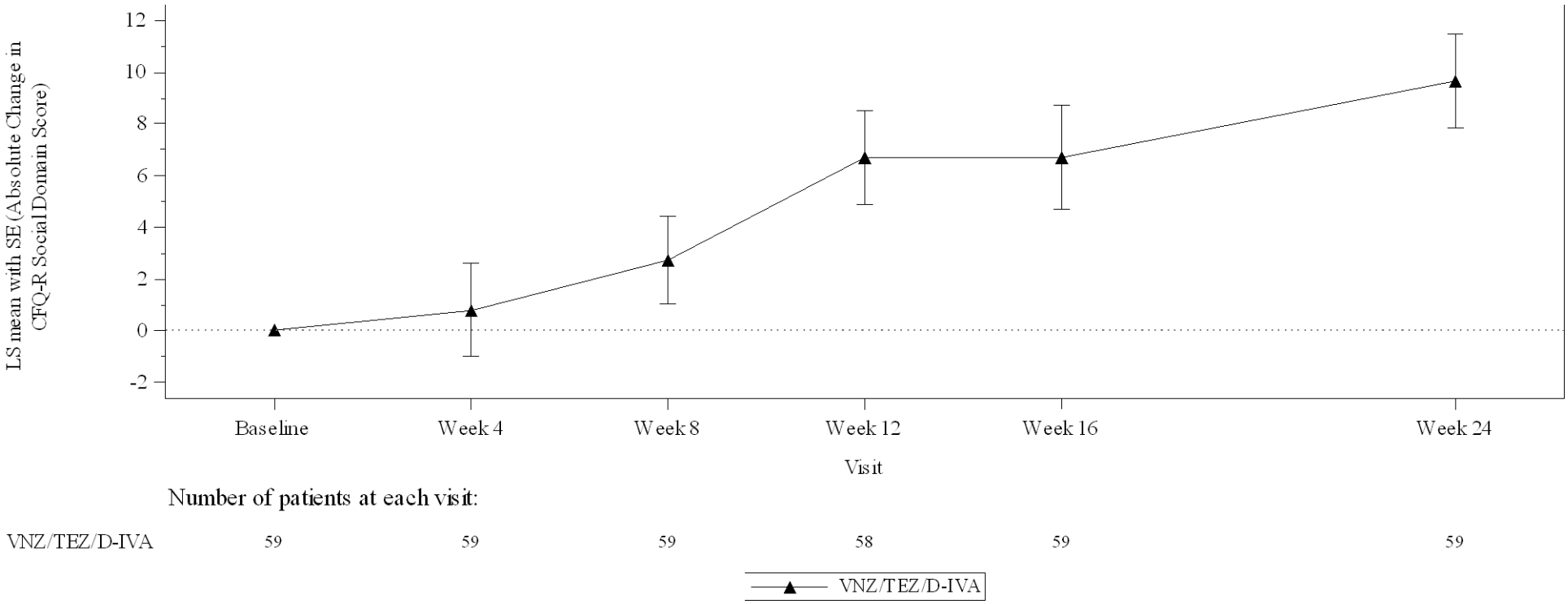
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Social
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

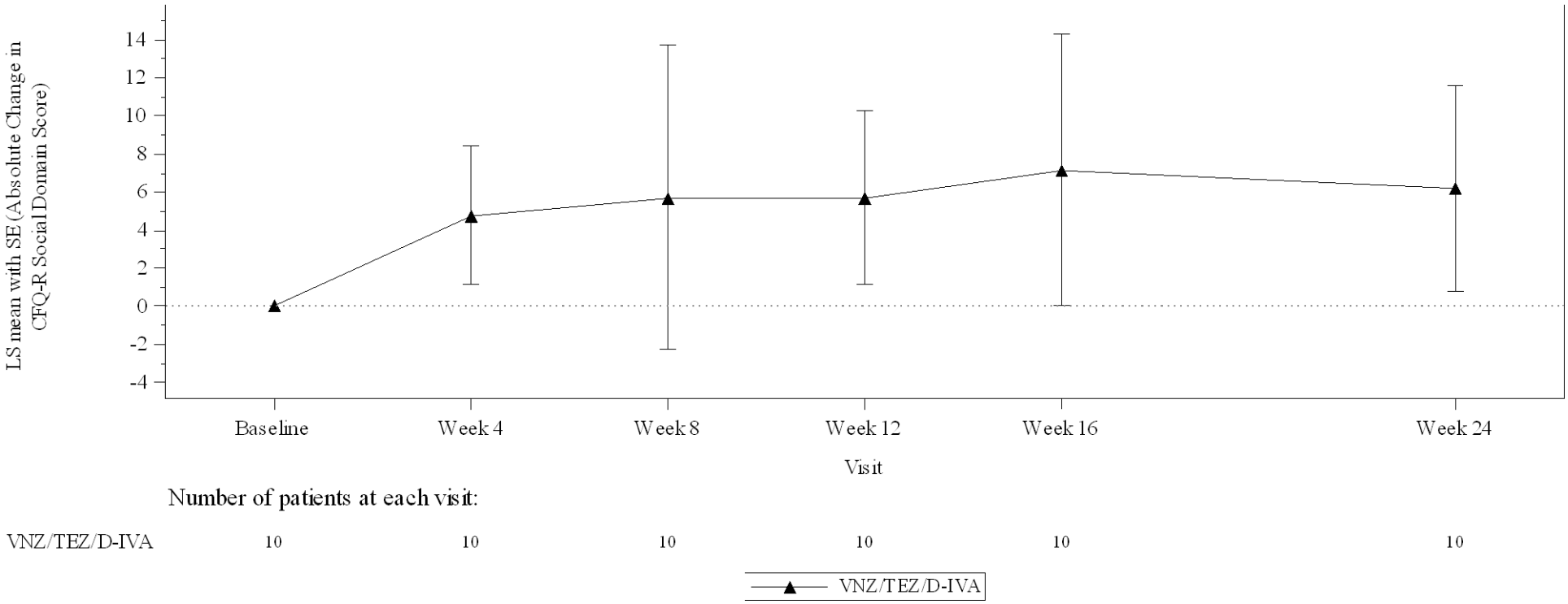
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Social
$LCI_{2.5}$ at baseline <7.5



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Social
$LCI_{2.5}$ at baseline ≥7.5



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

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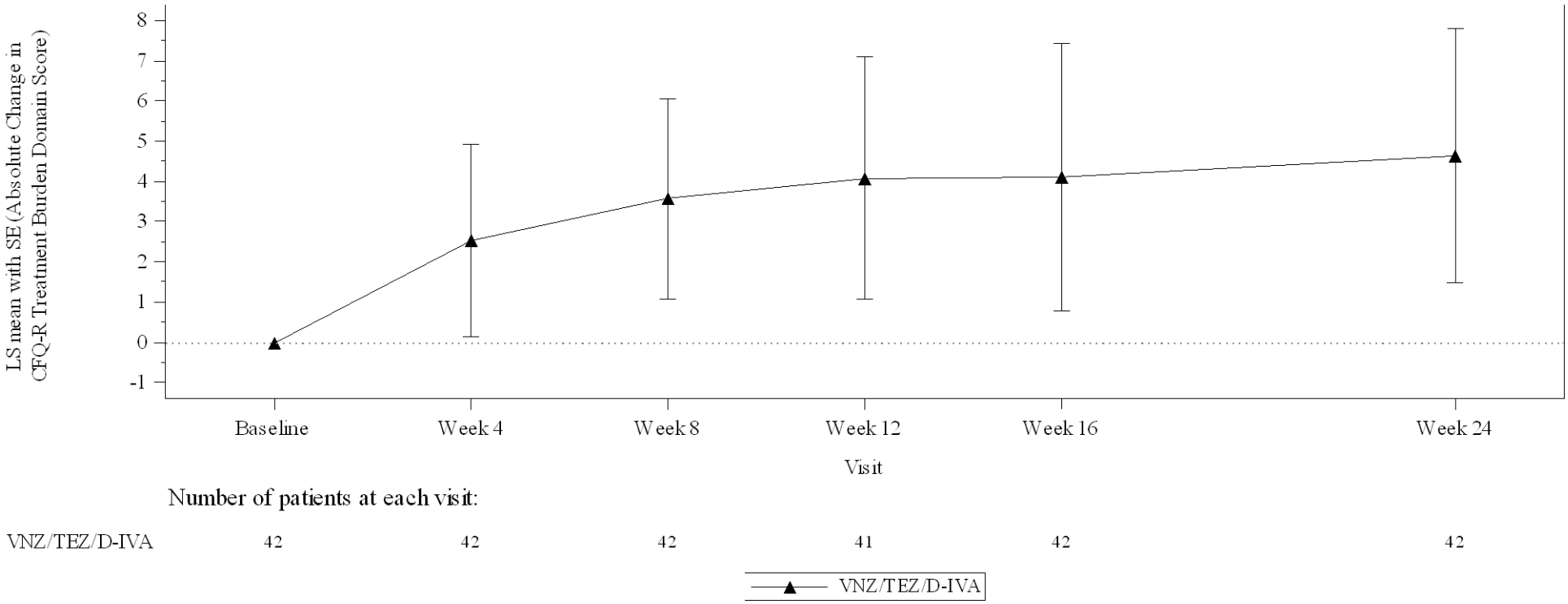
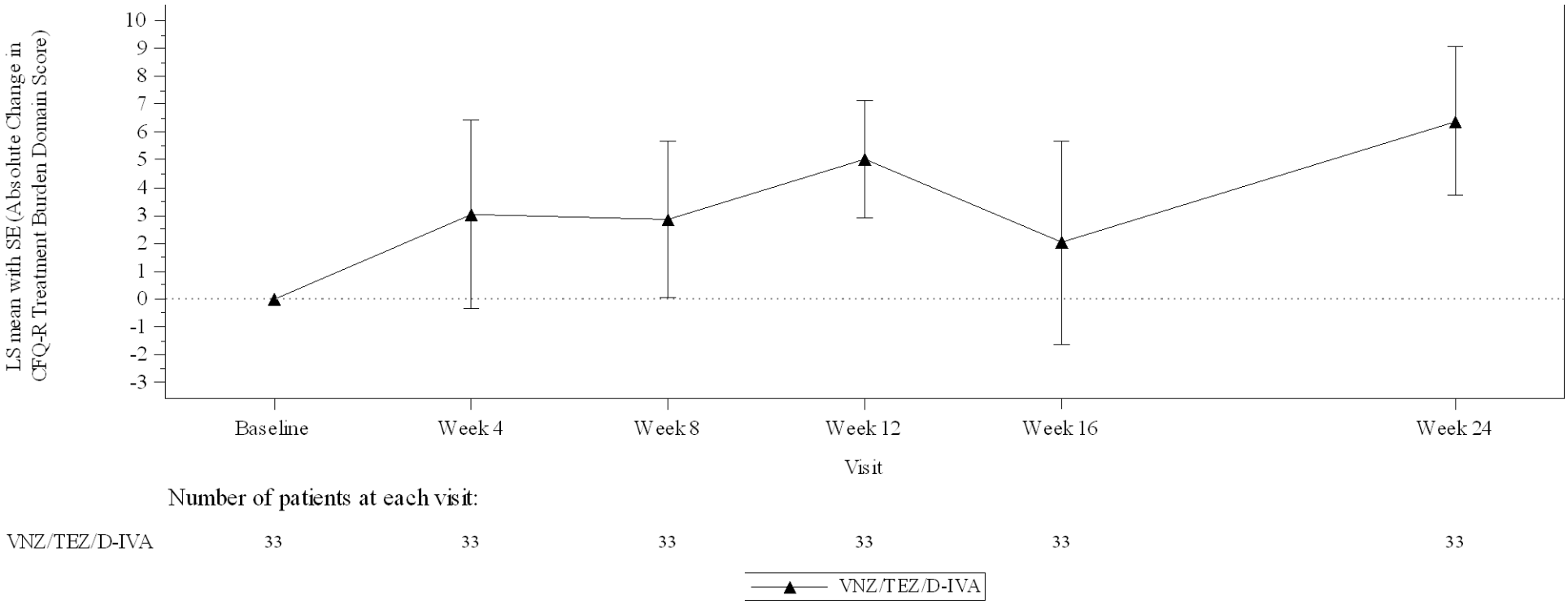
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

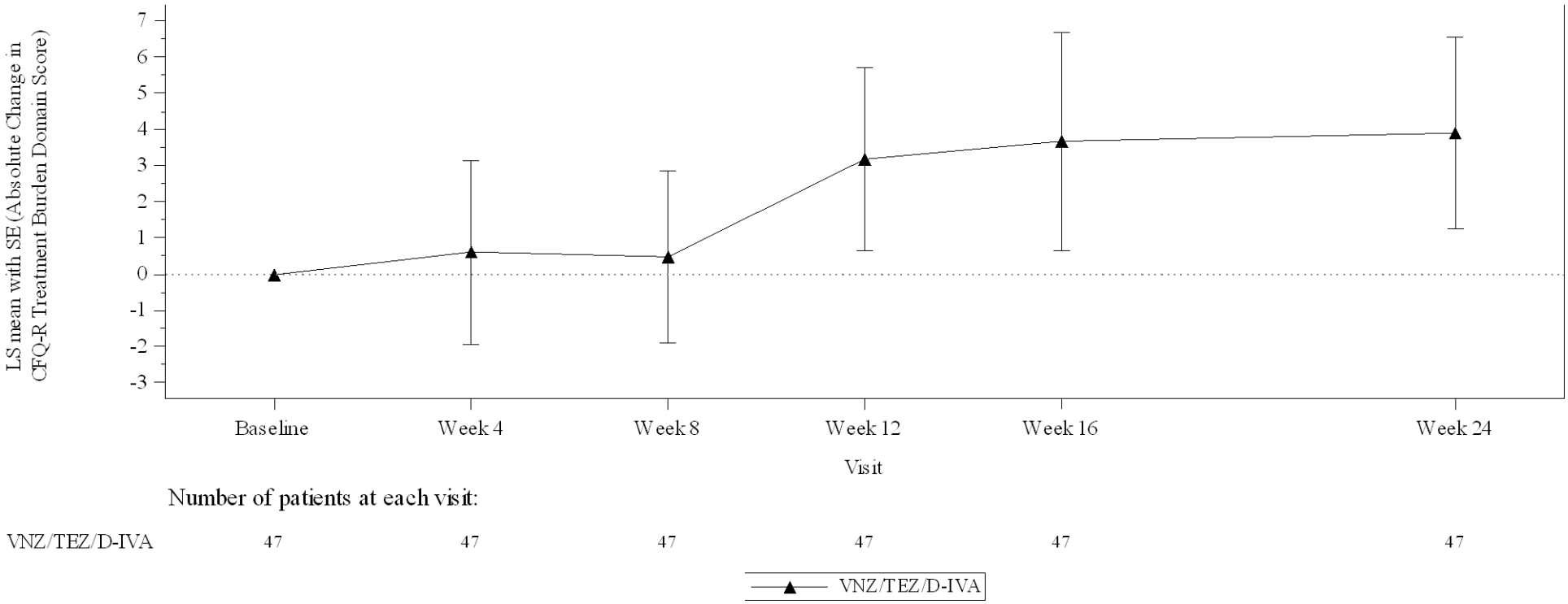
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

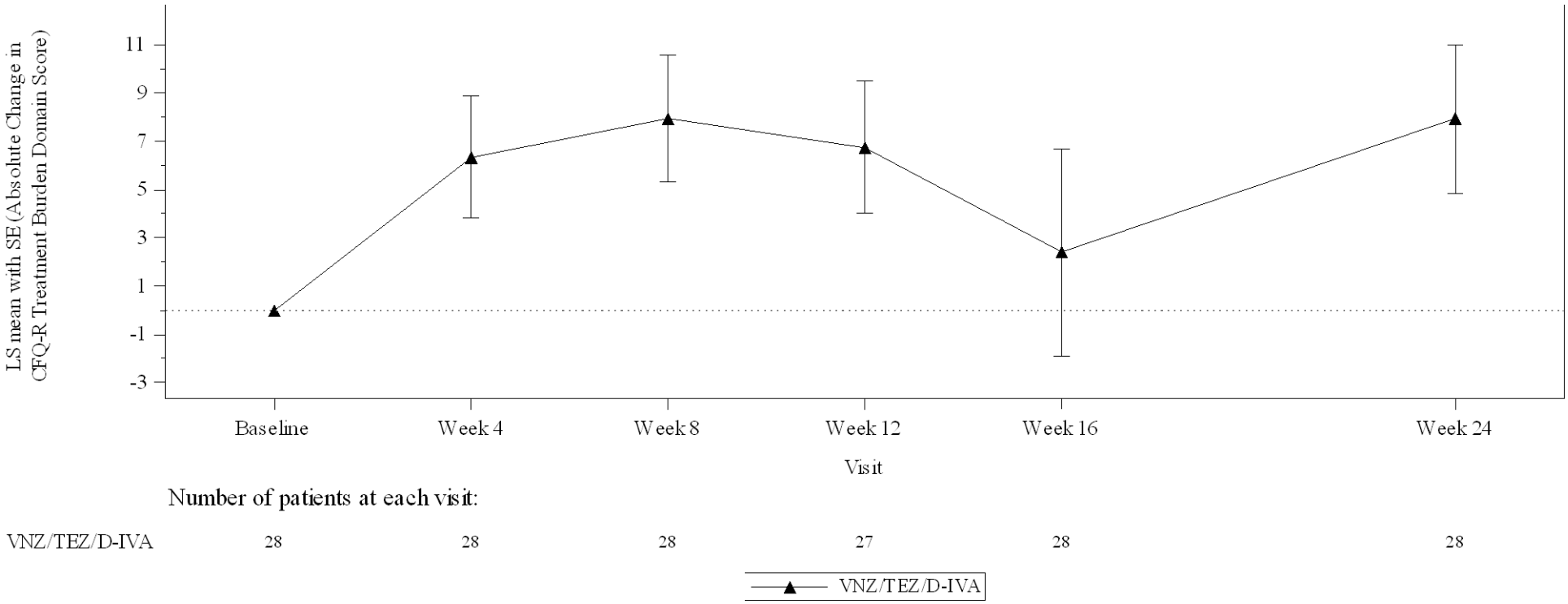
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

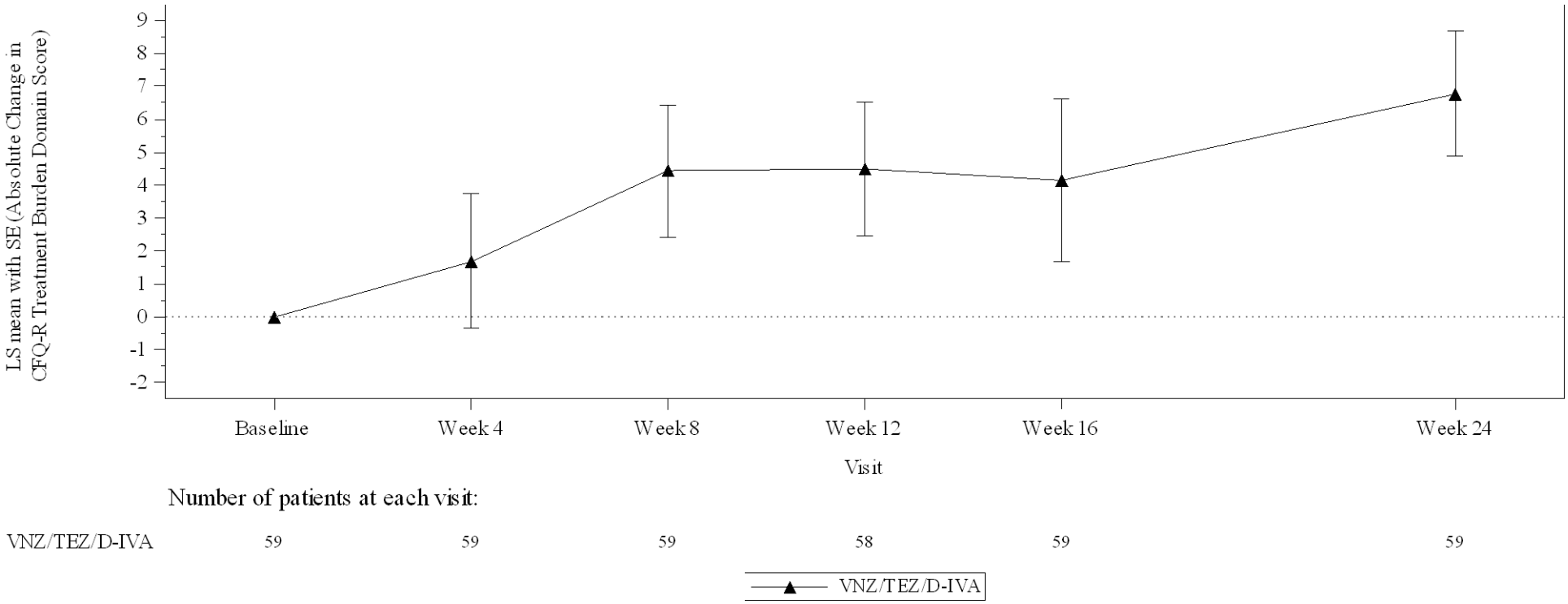
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

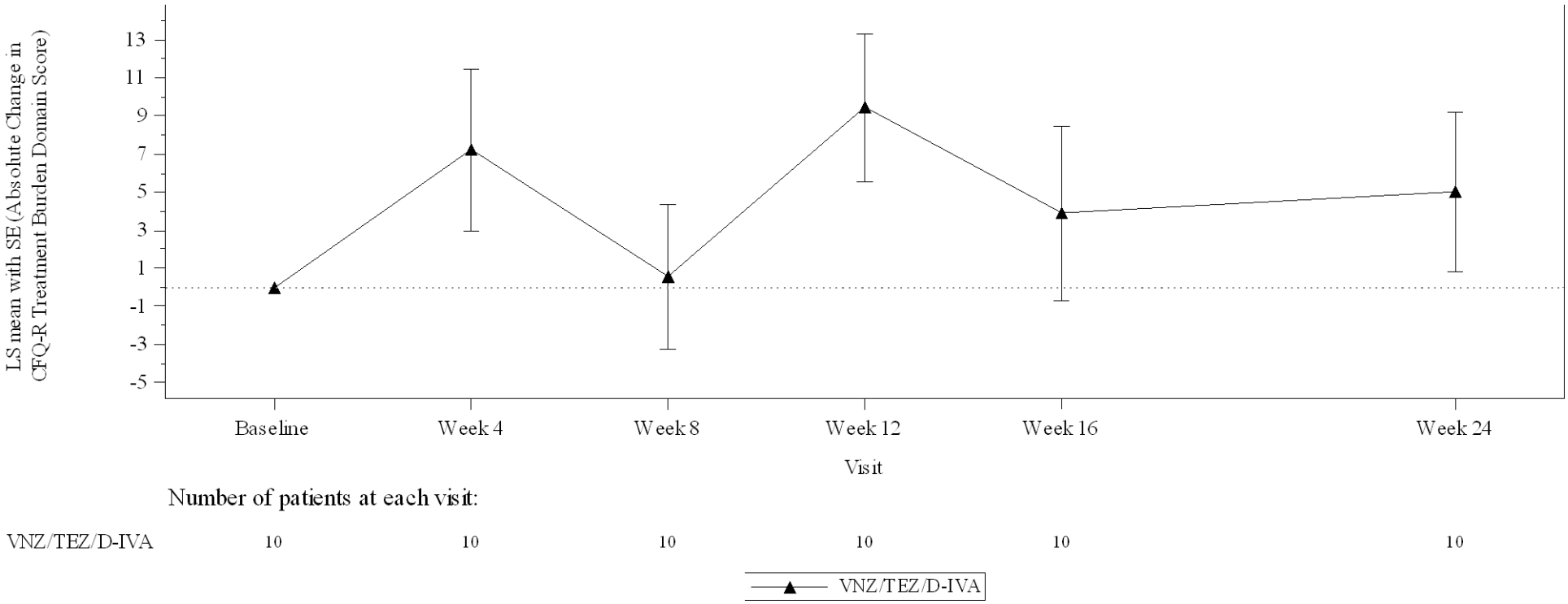
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden
$LCI_{2.5}$ at baseline <7.5



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

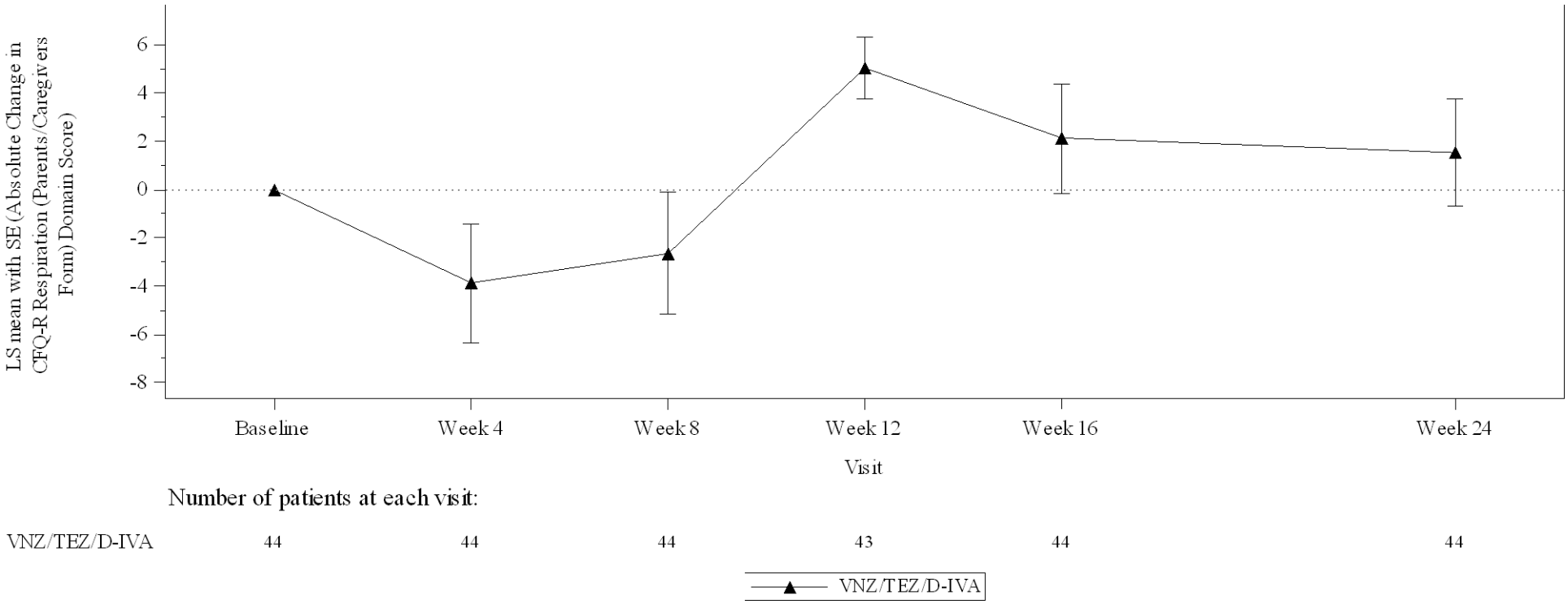
Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden
$LCI_{2.5}$ at baseline ≥7.5



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

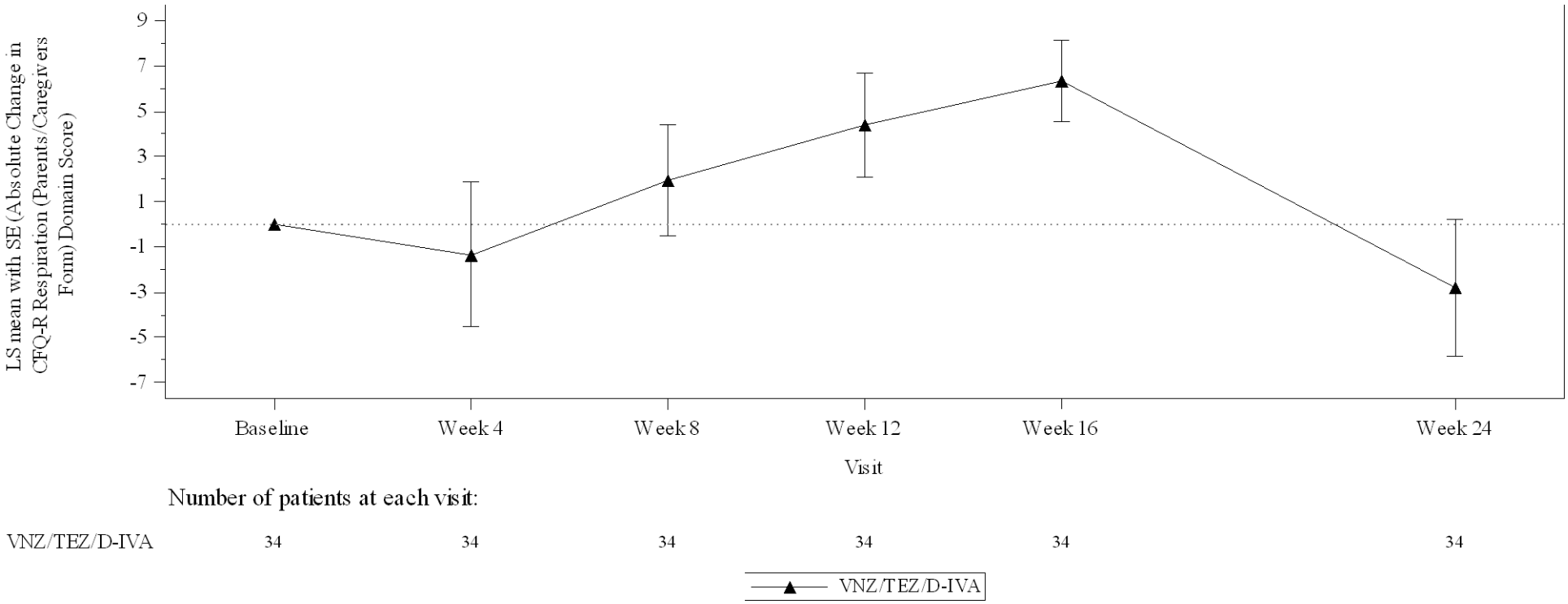
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-ch-24wks-sub-b1.sas Creation: 06FEB2025 10:21

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Sex = Male



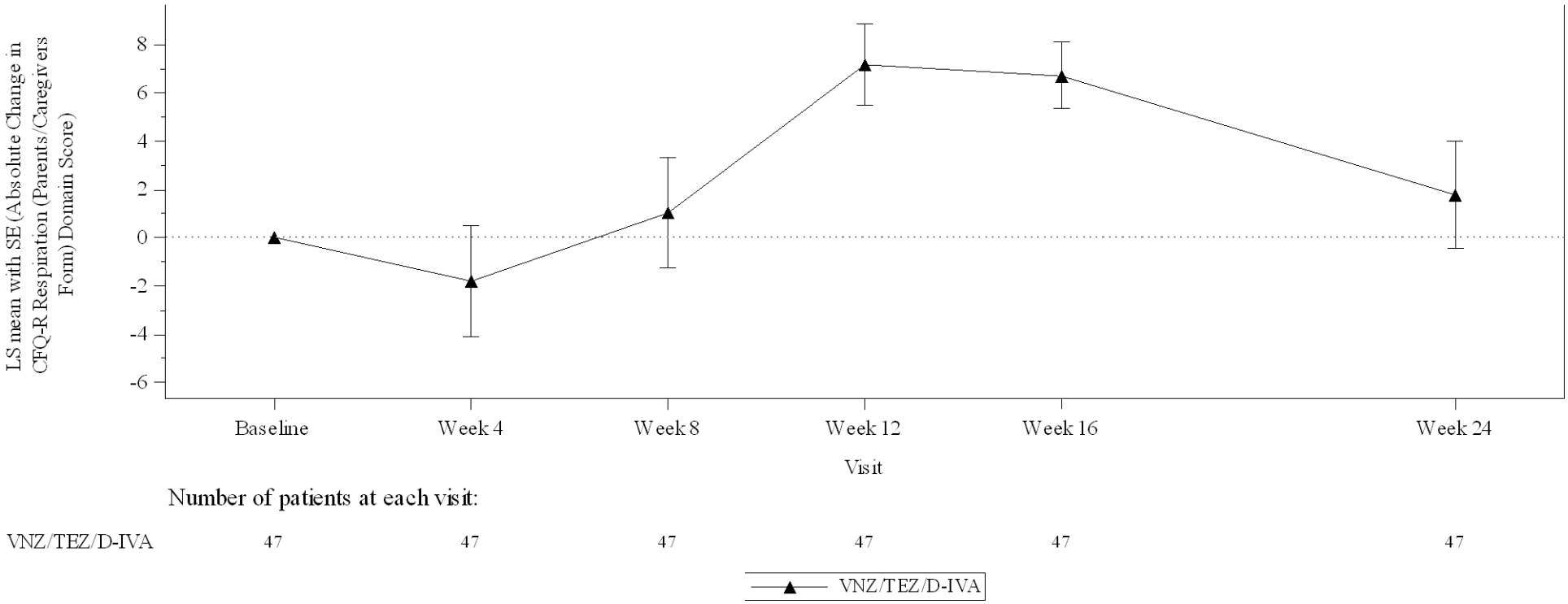
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Region = North America



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- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Region = Rest of World

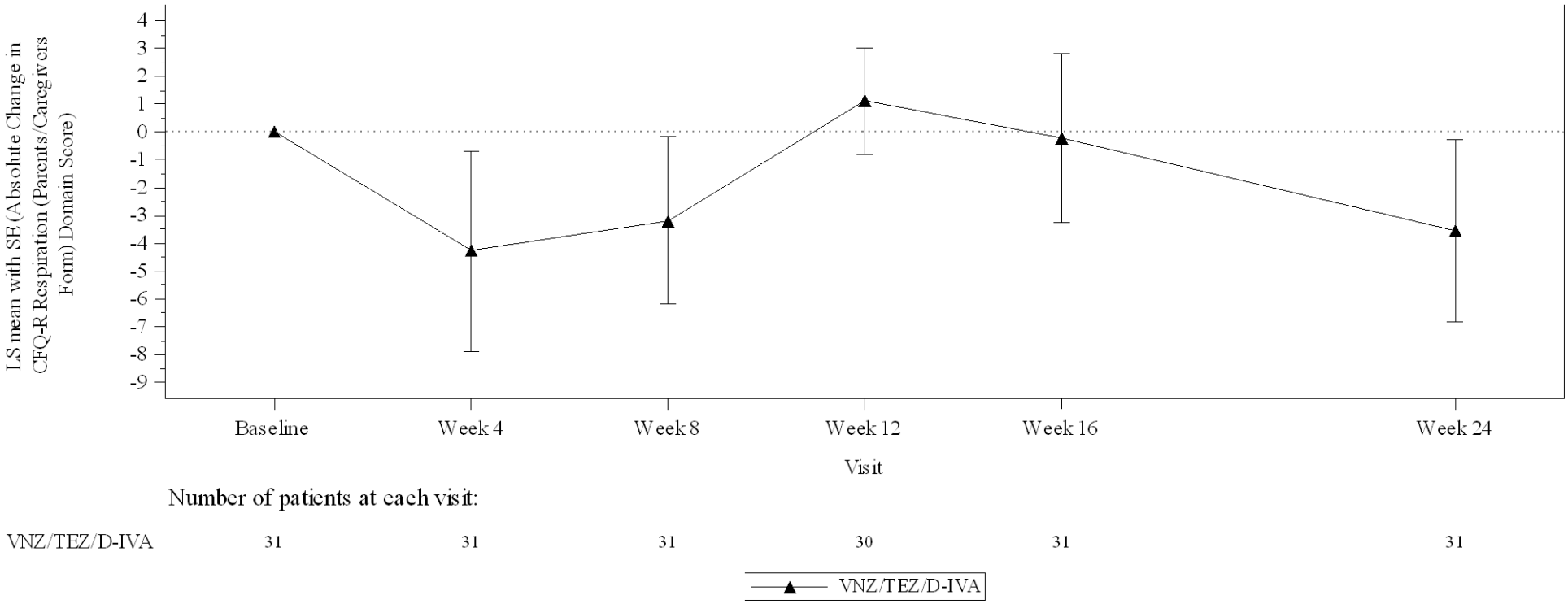

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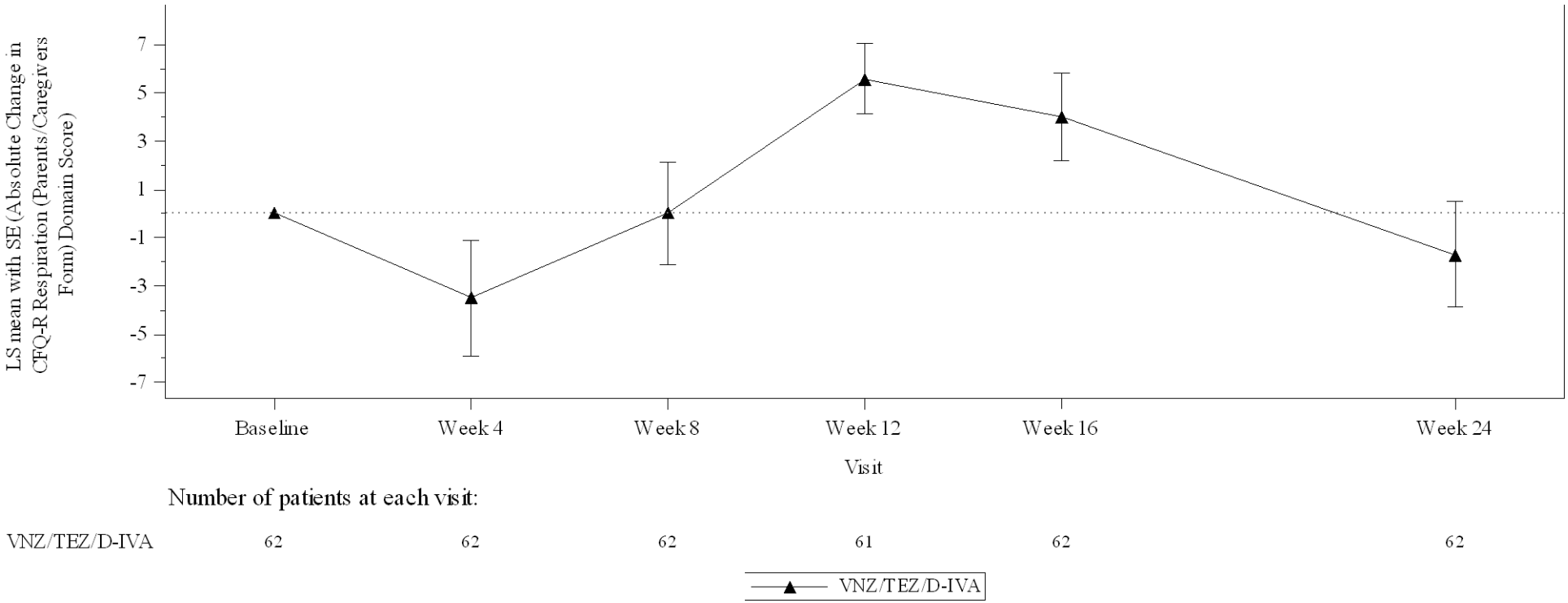
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5



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- Baseline is defined as the pre-dose Day 1 value.
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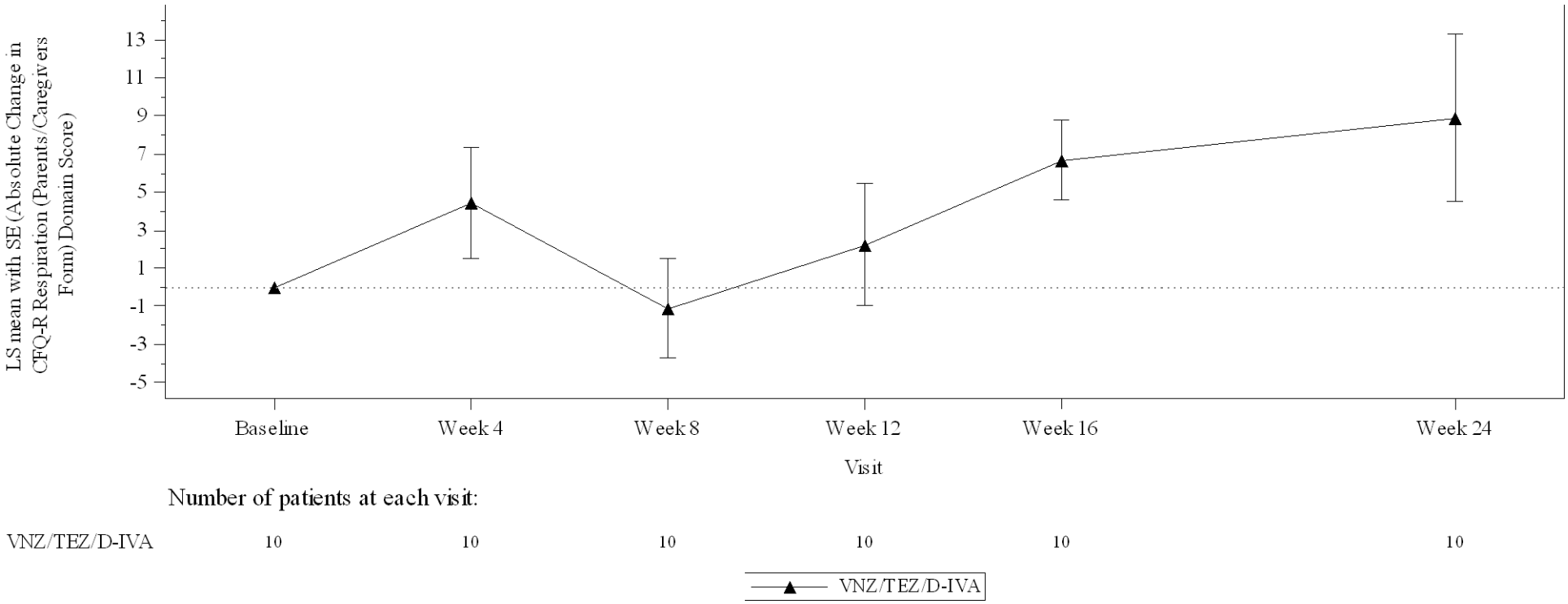
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5



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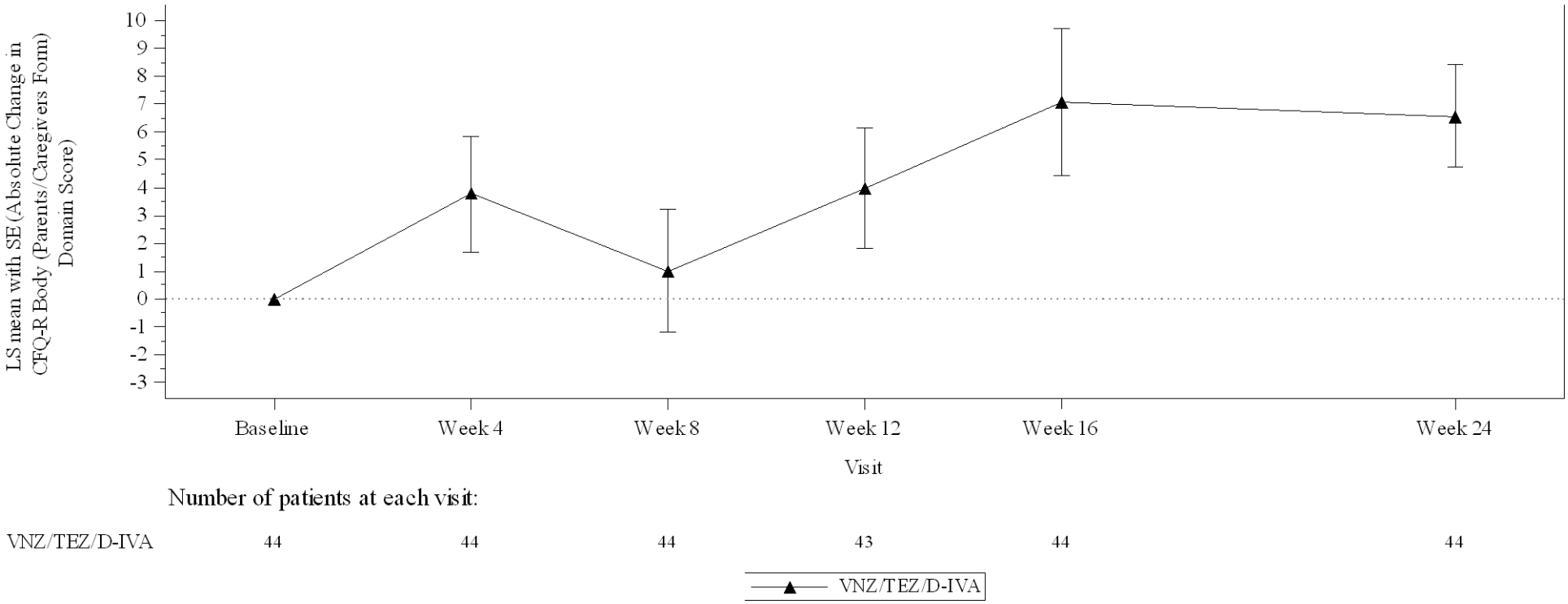
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Sex = Male



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- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

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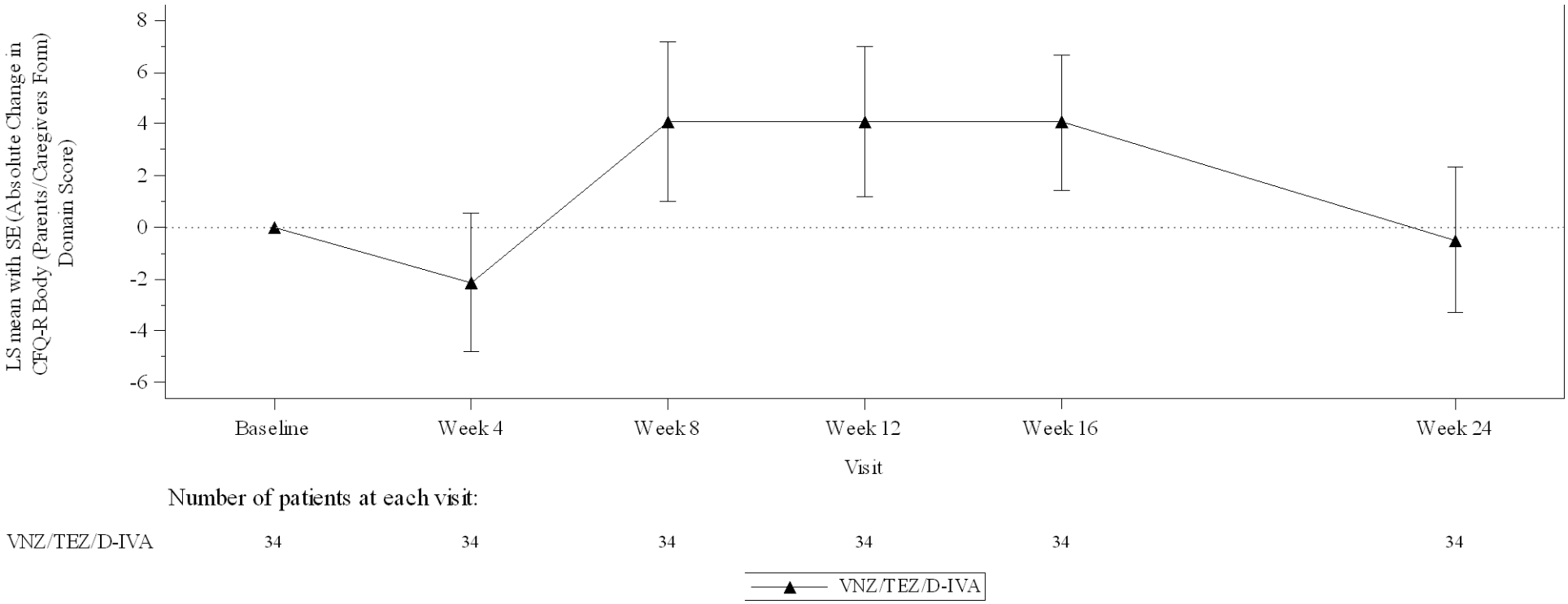
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Region = North America

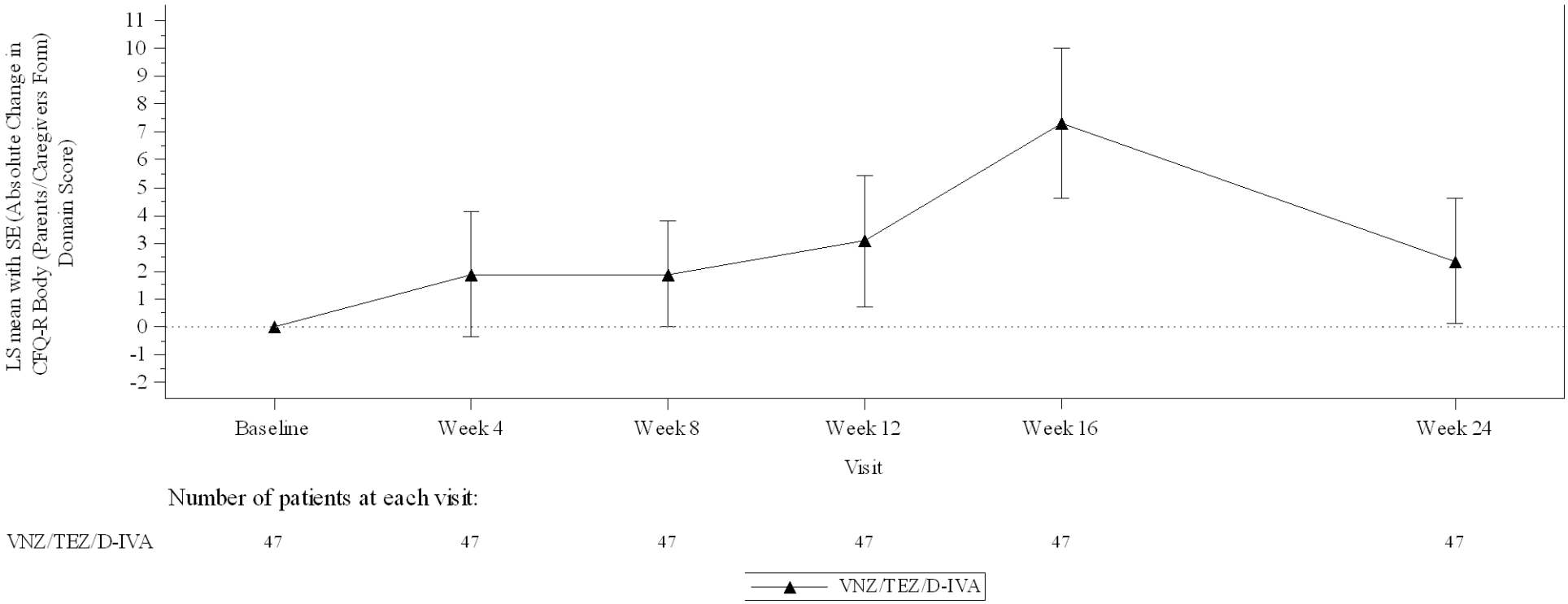

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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Region = Rest of World

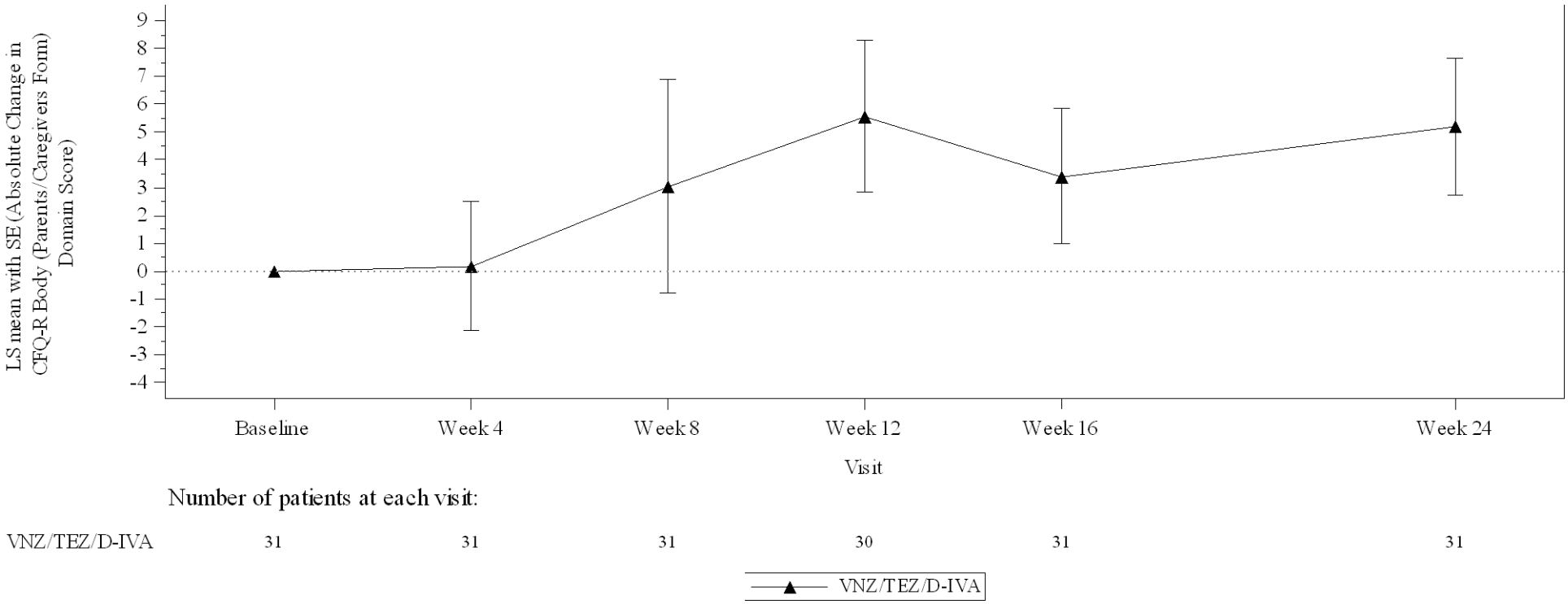

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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

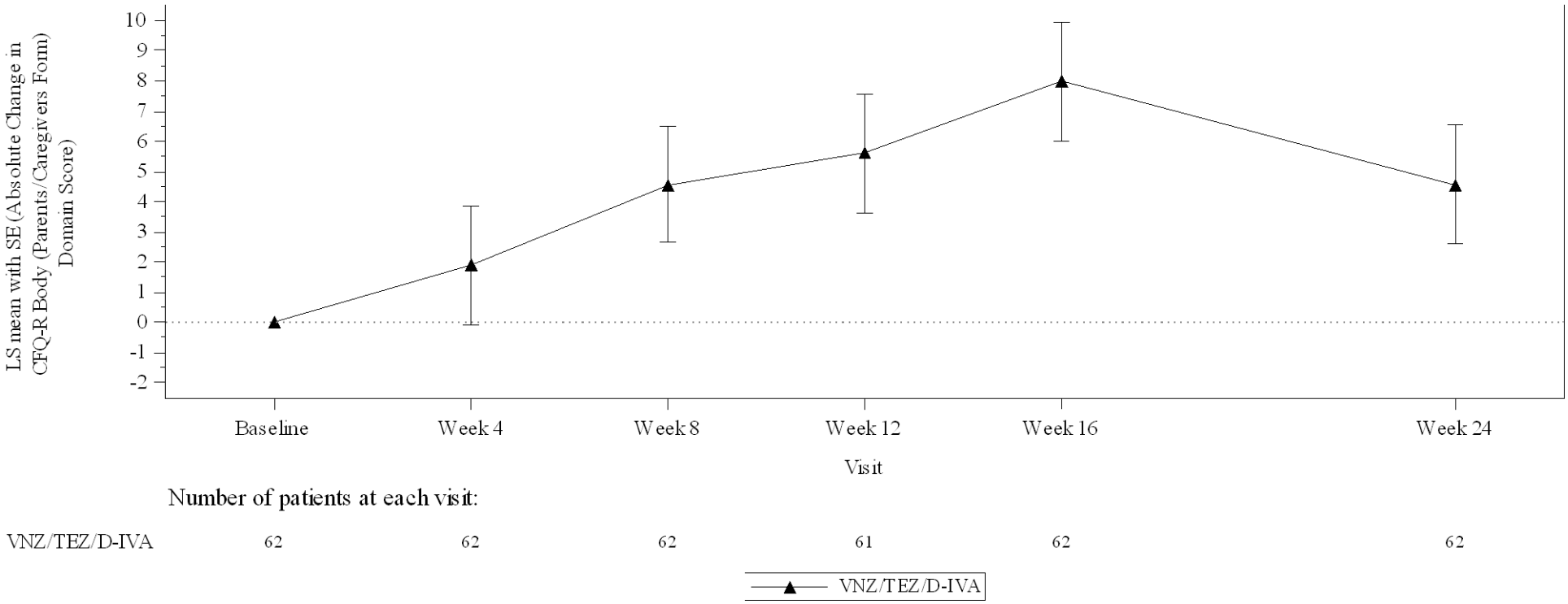

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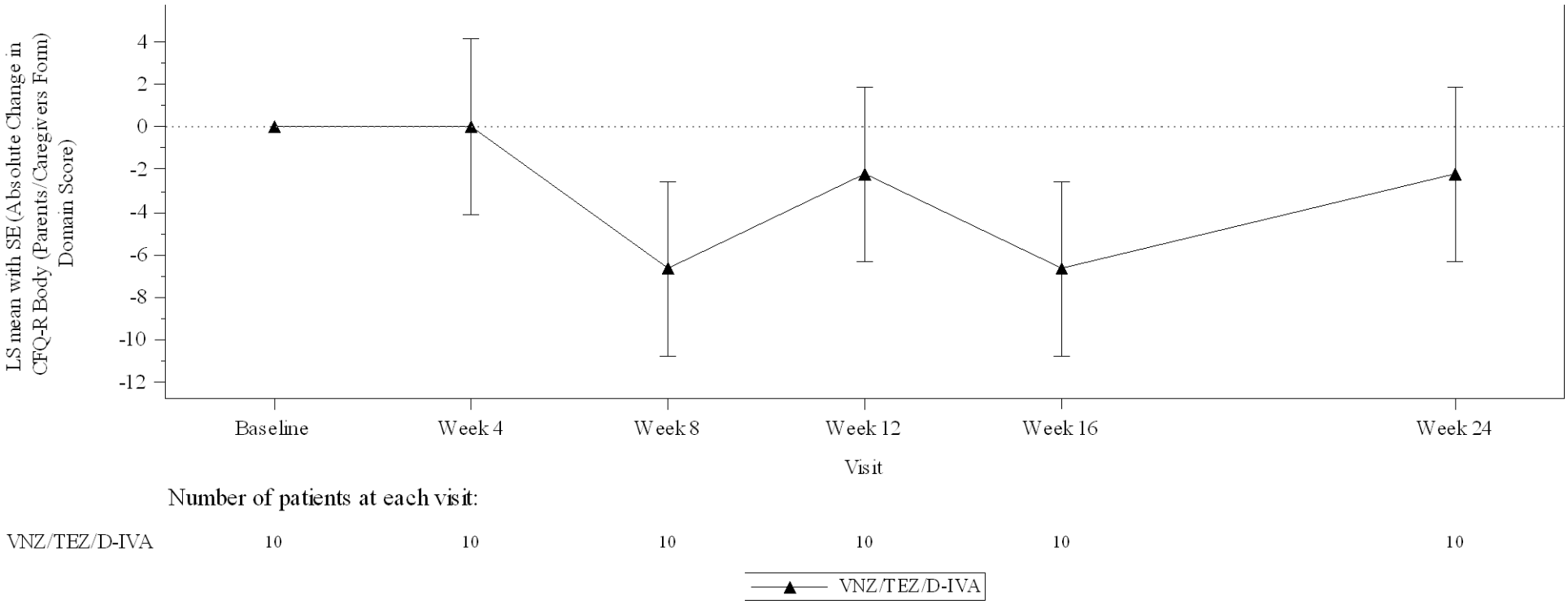
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5



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- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Sex = Male

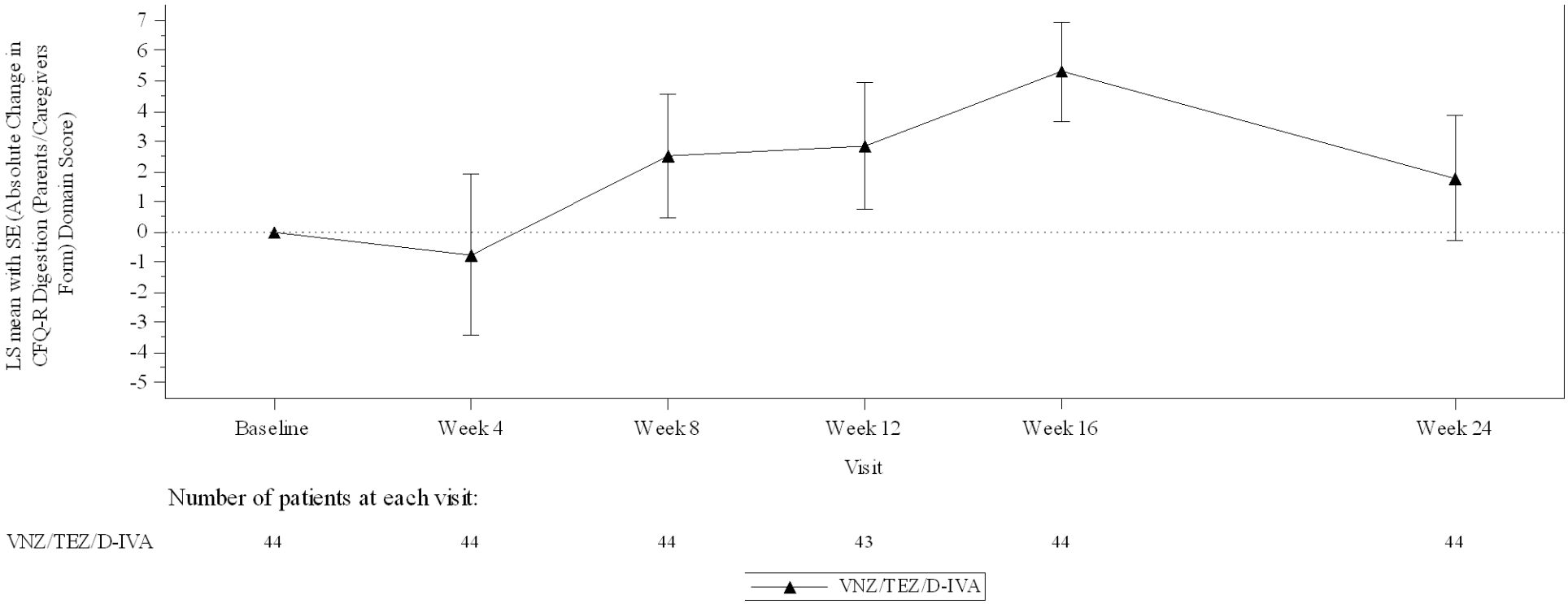

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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Sex = Female

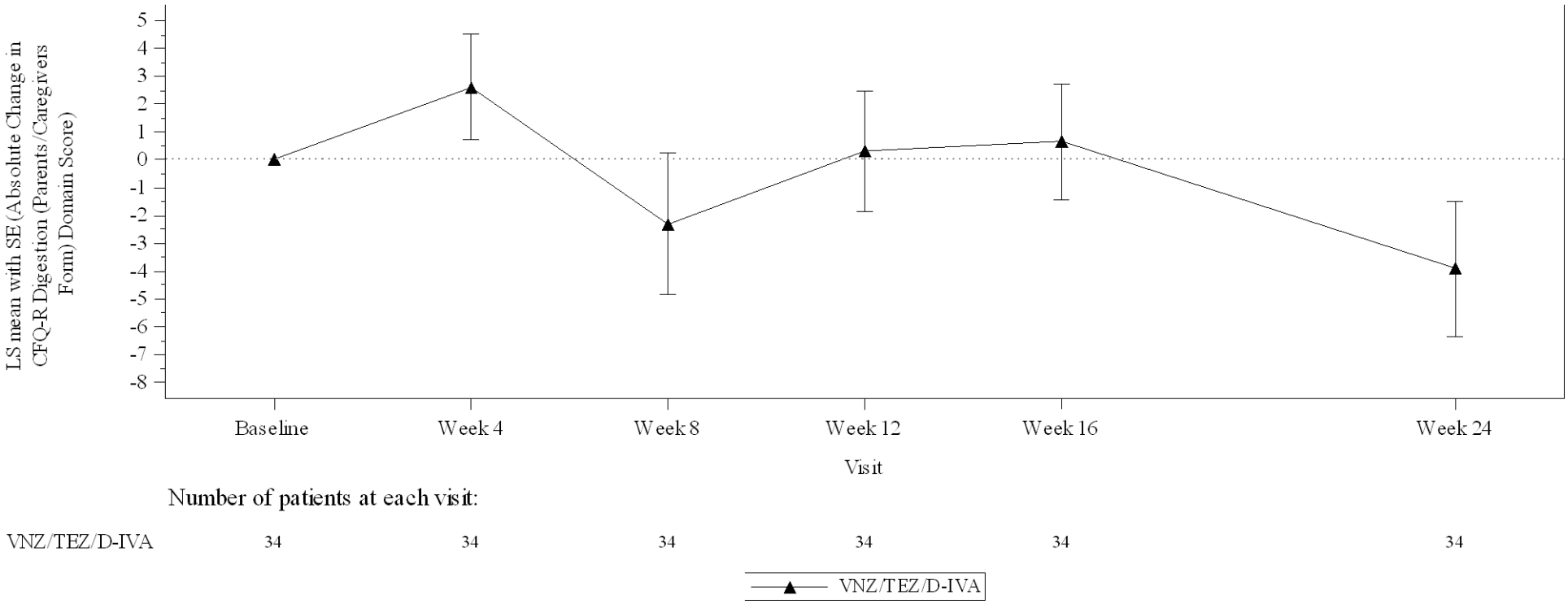

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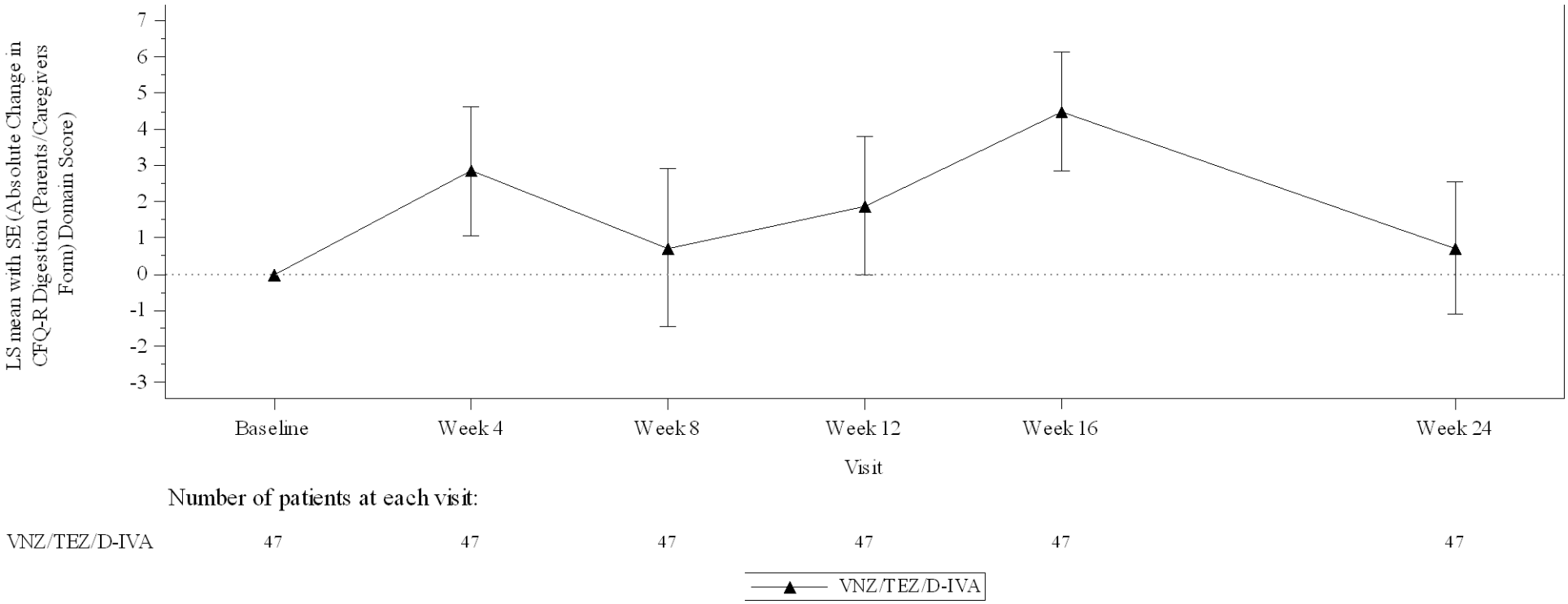
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Region = North America



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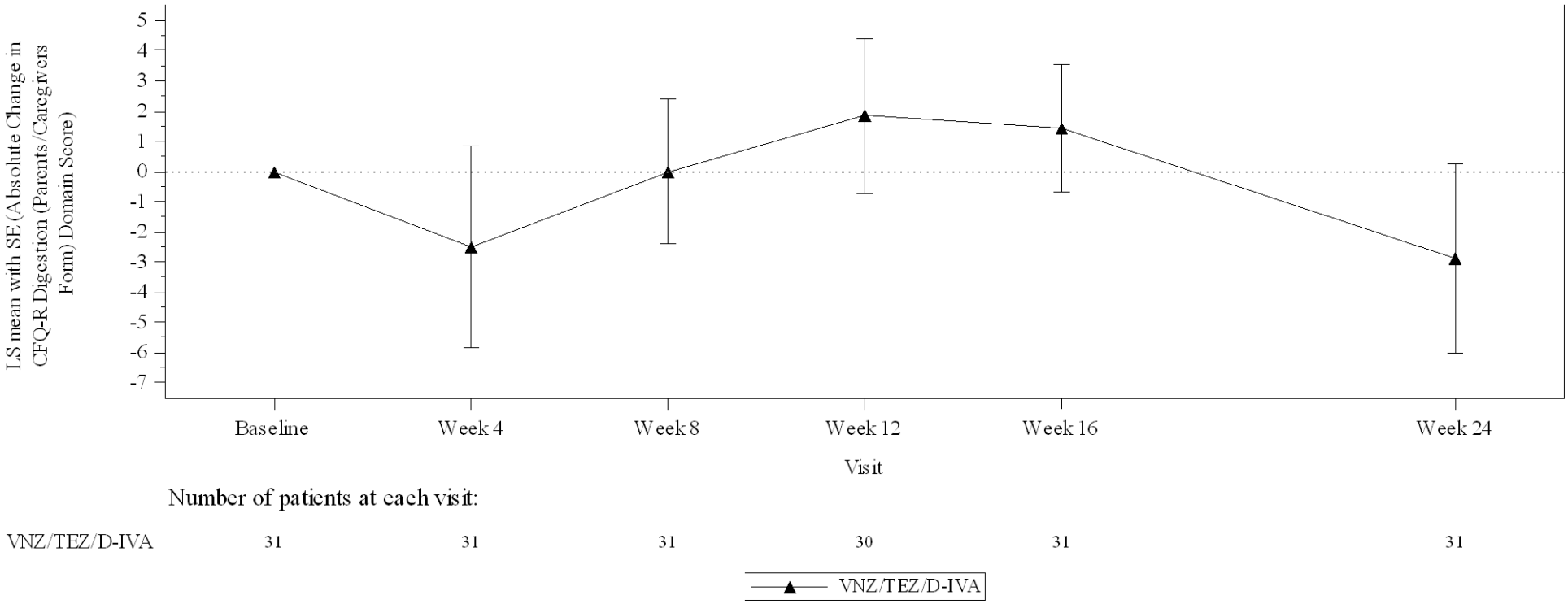
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World



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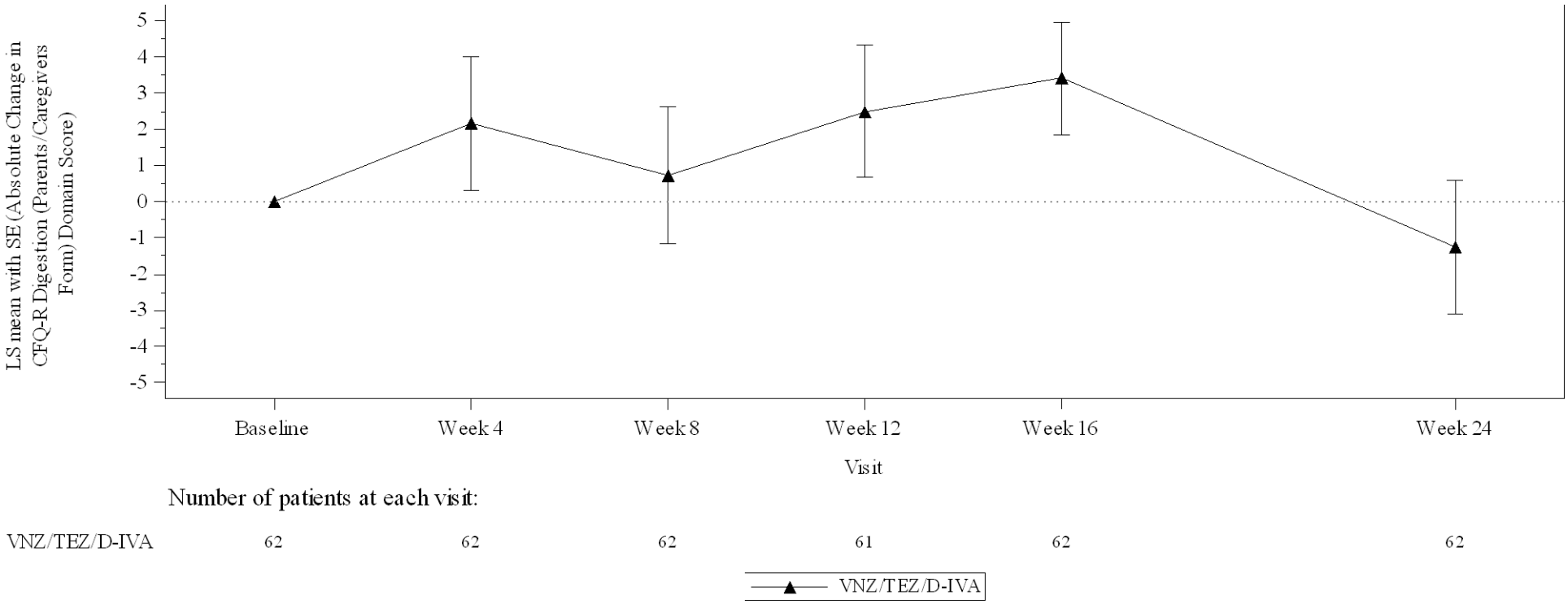
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5



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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

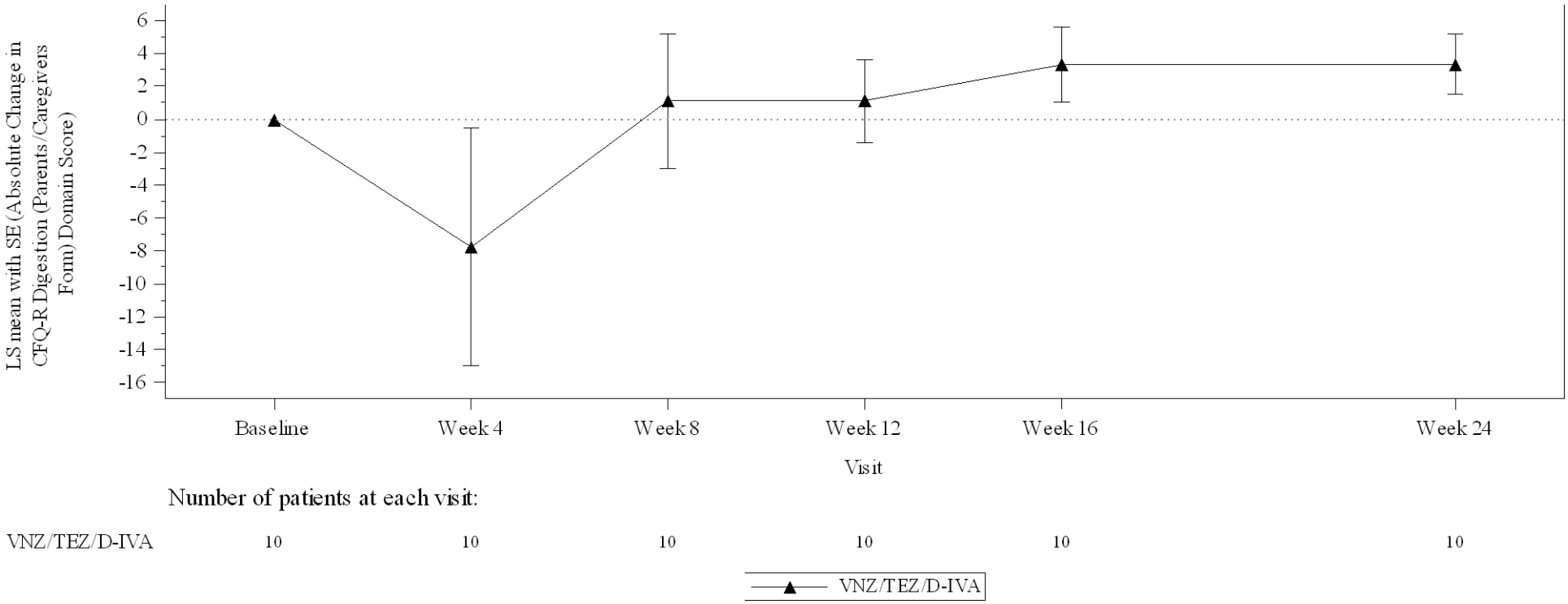

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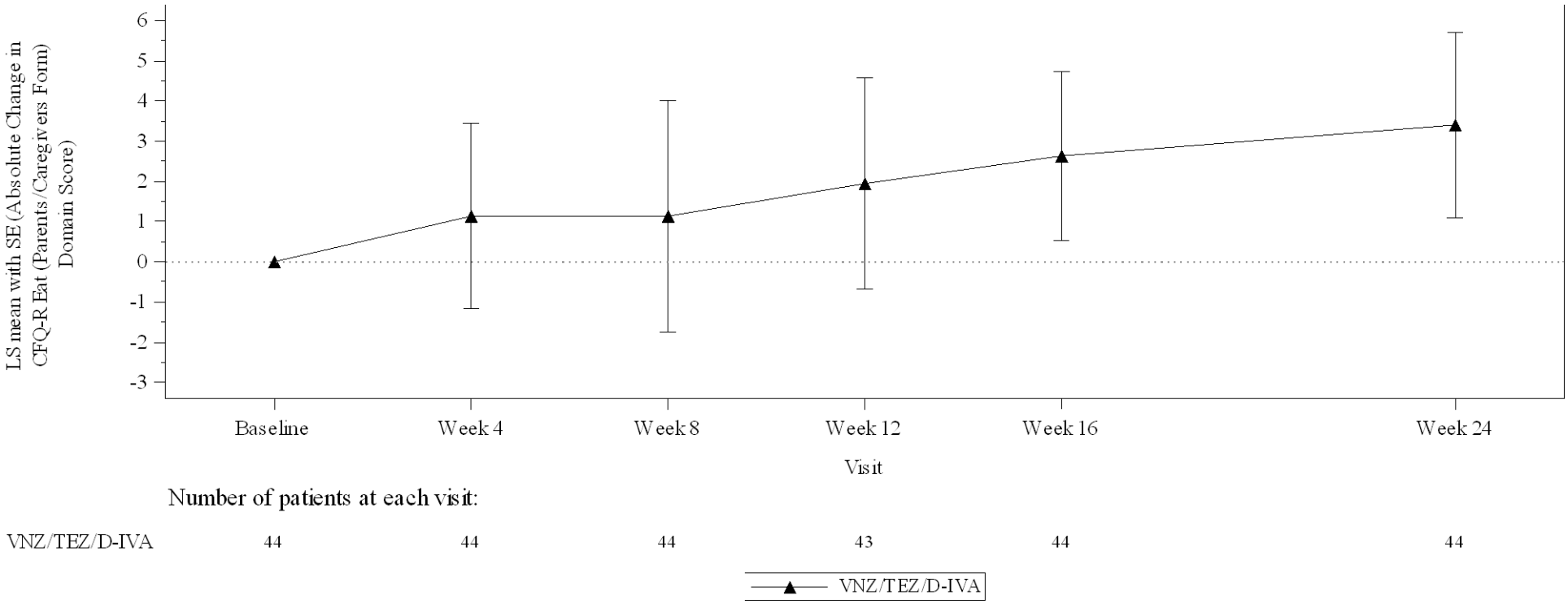
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Sex = Male



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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Sex = Female

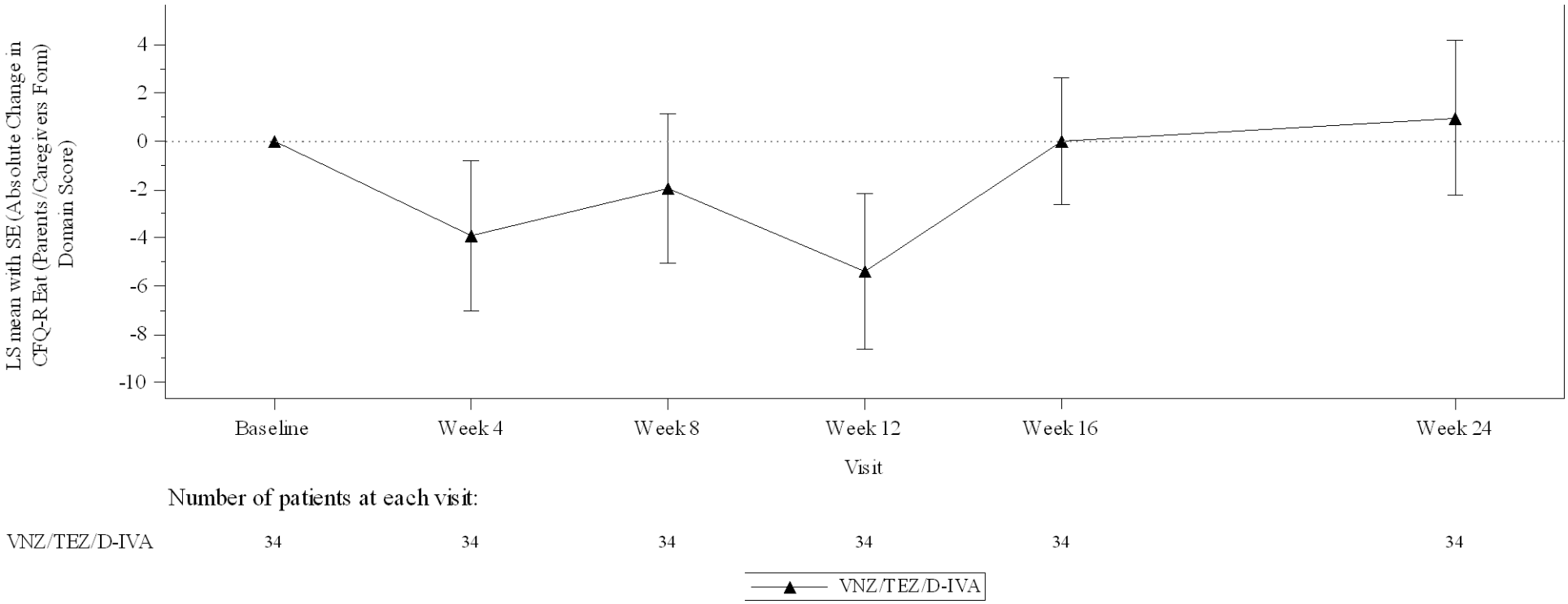

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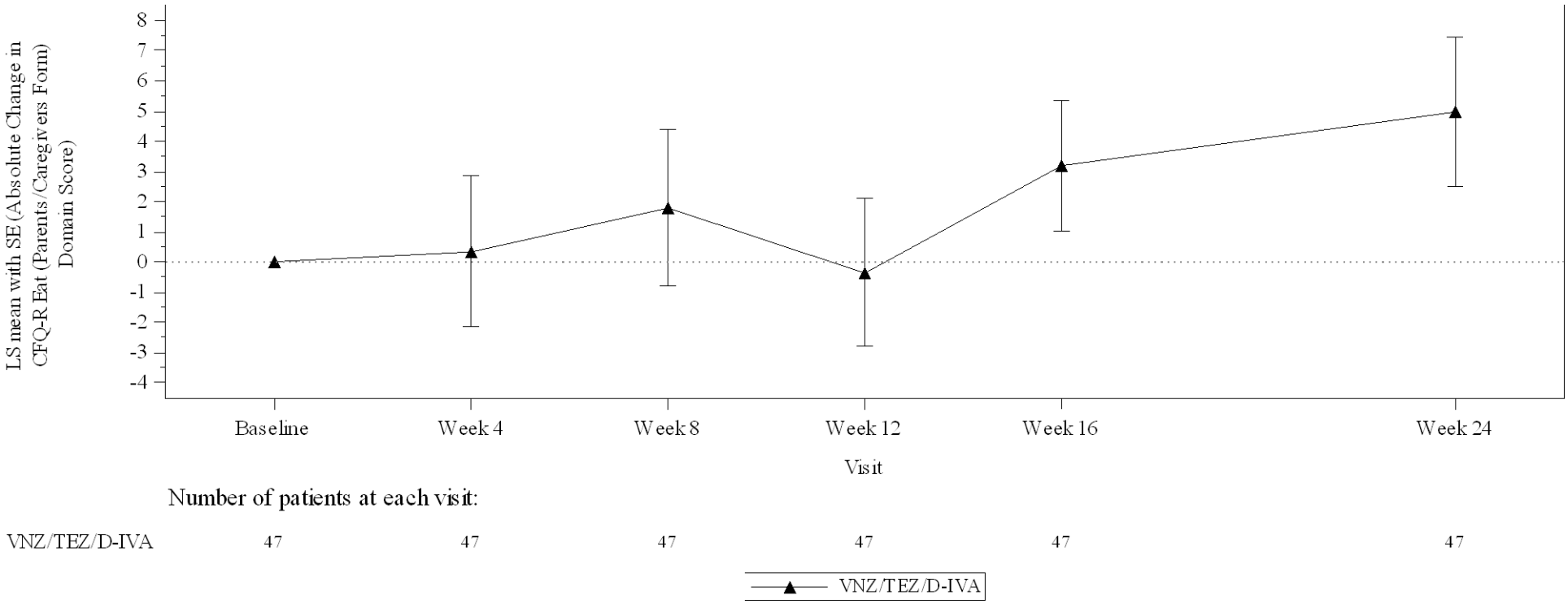
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

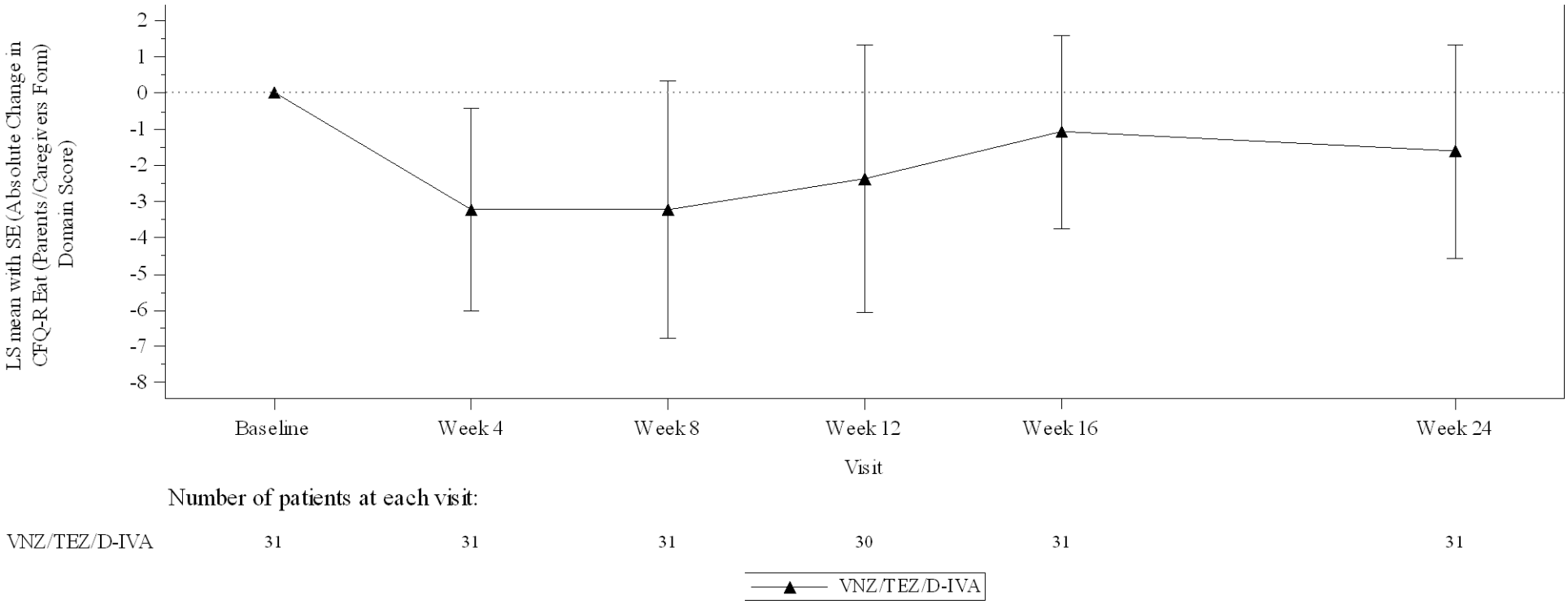


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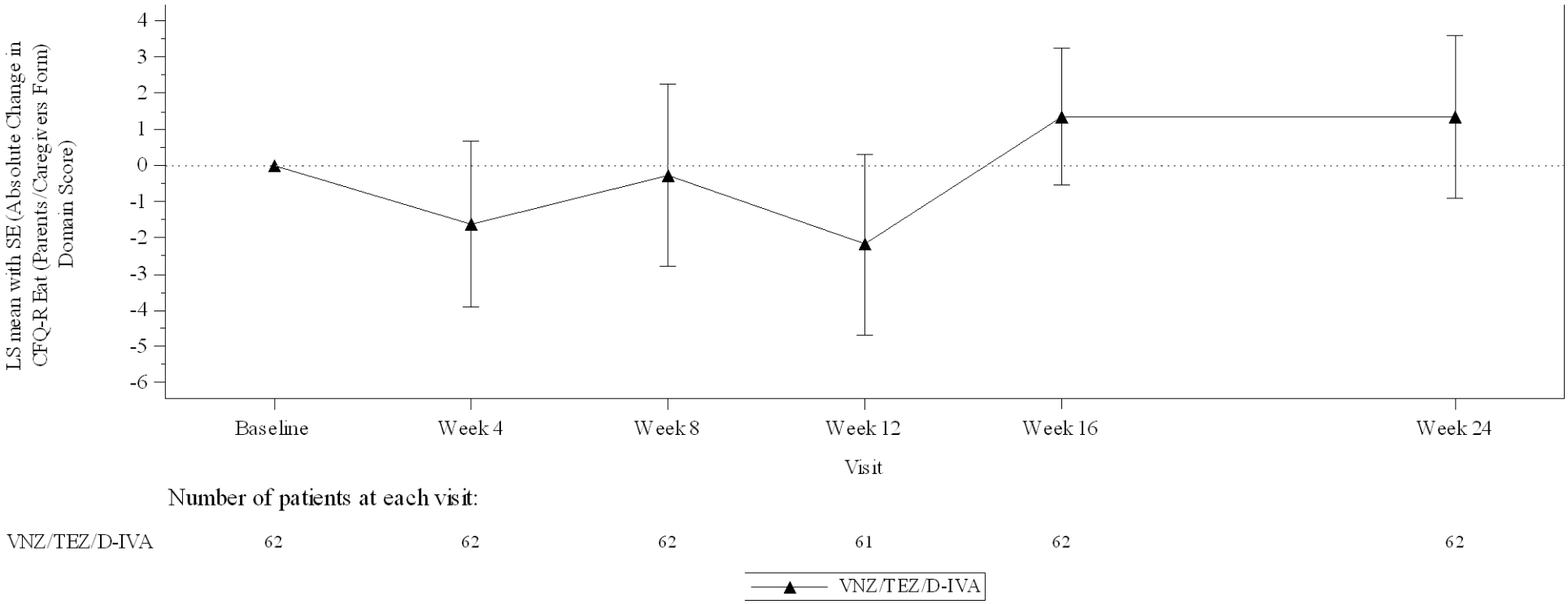
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5



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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

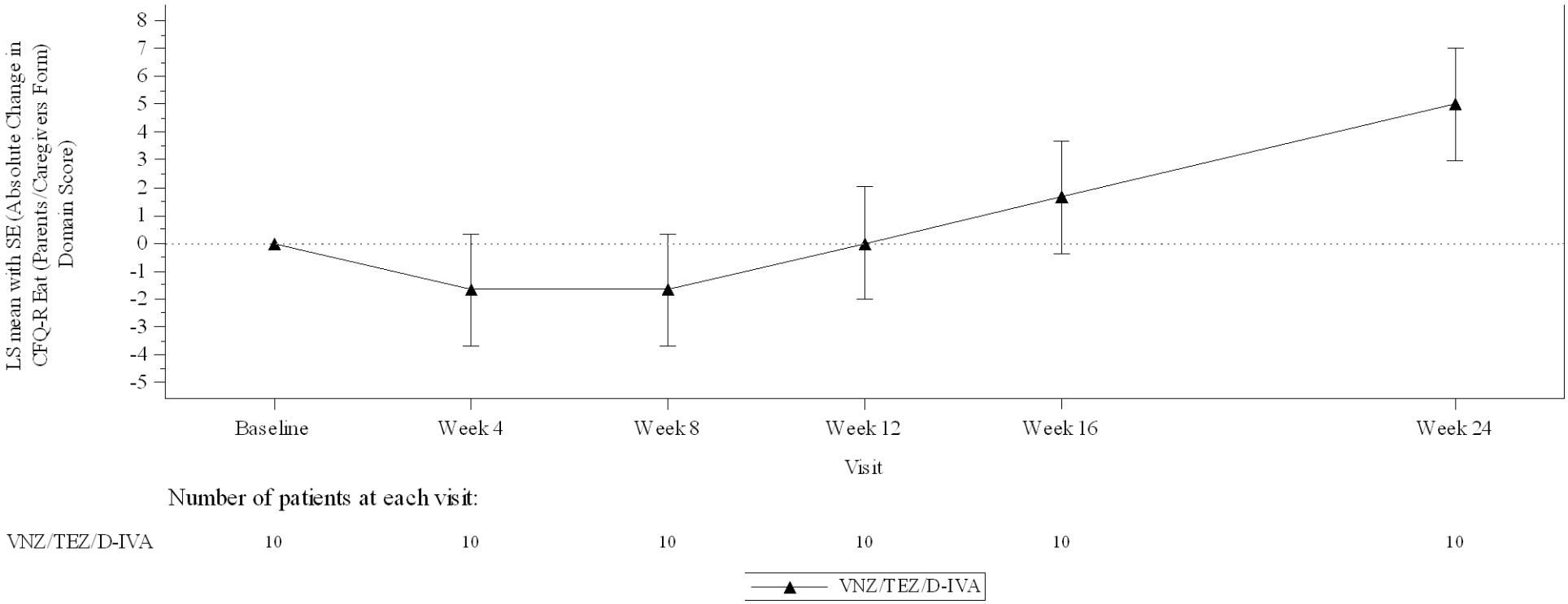

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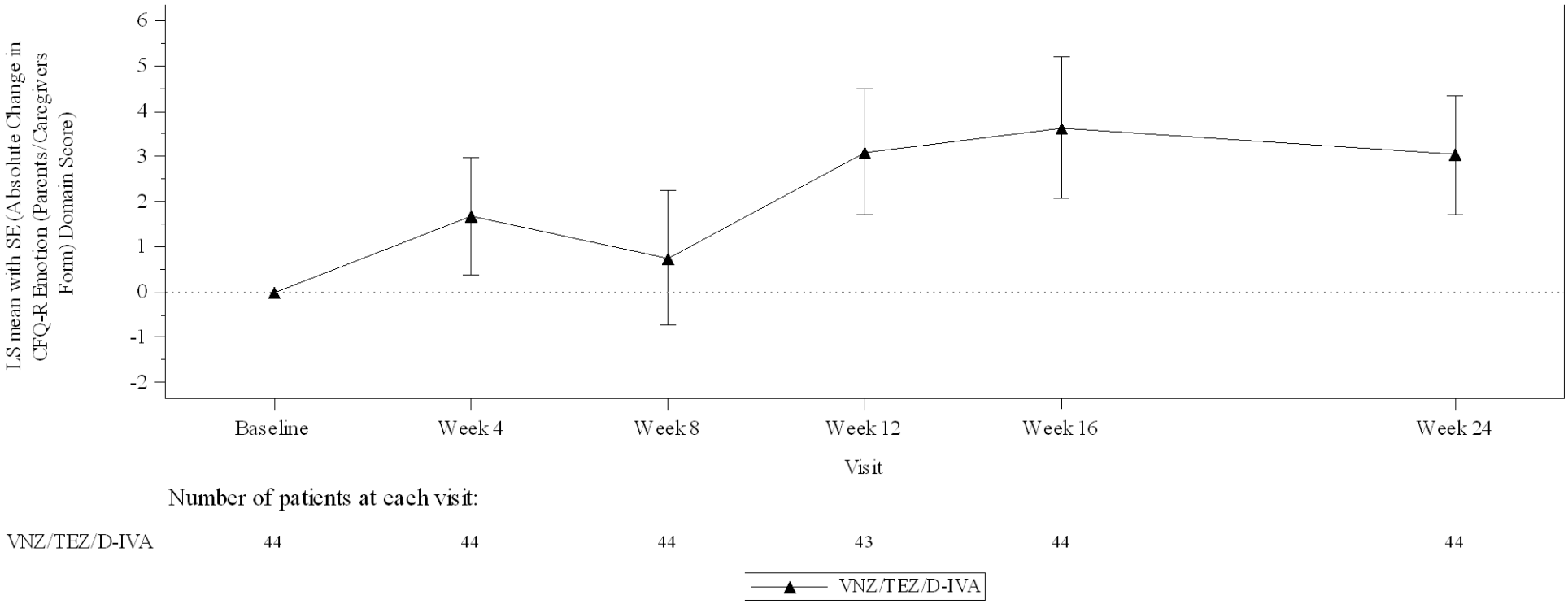
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Sex = Male



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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Sex = Female

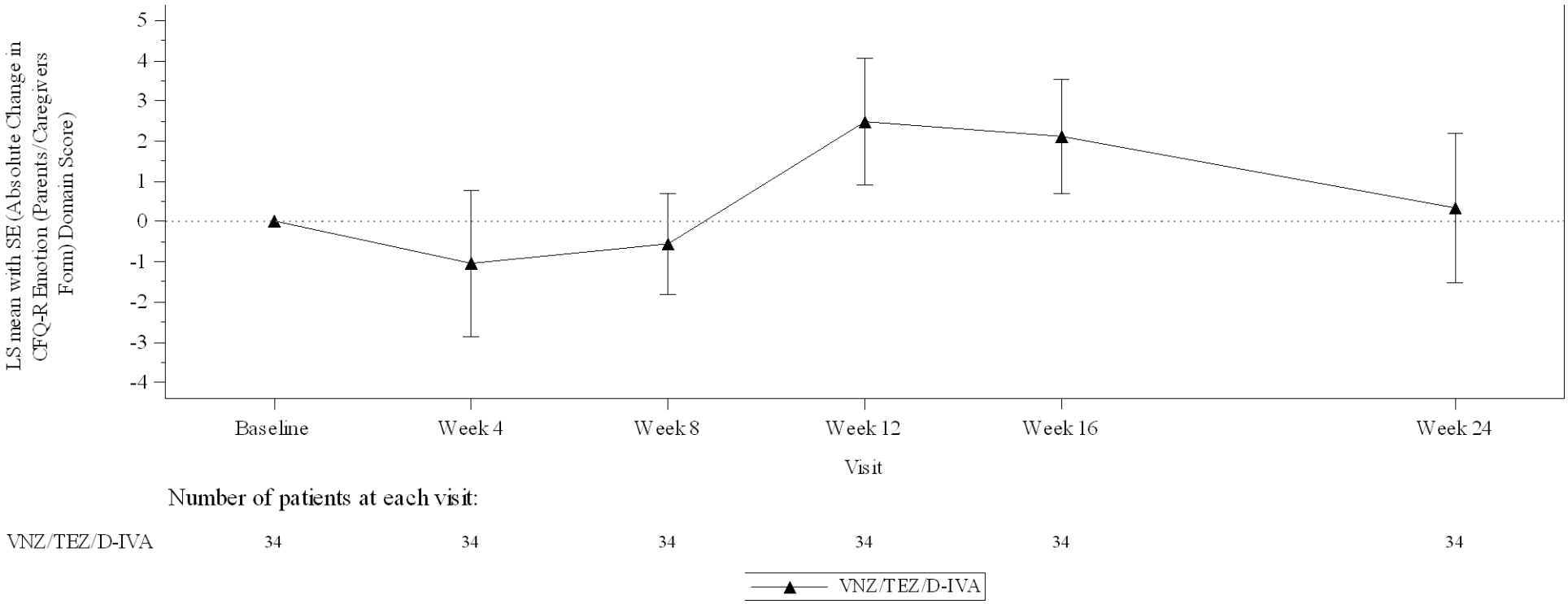

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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Region = North America

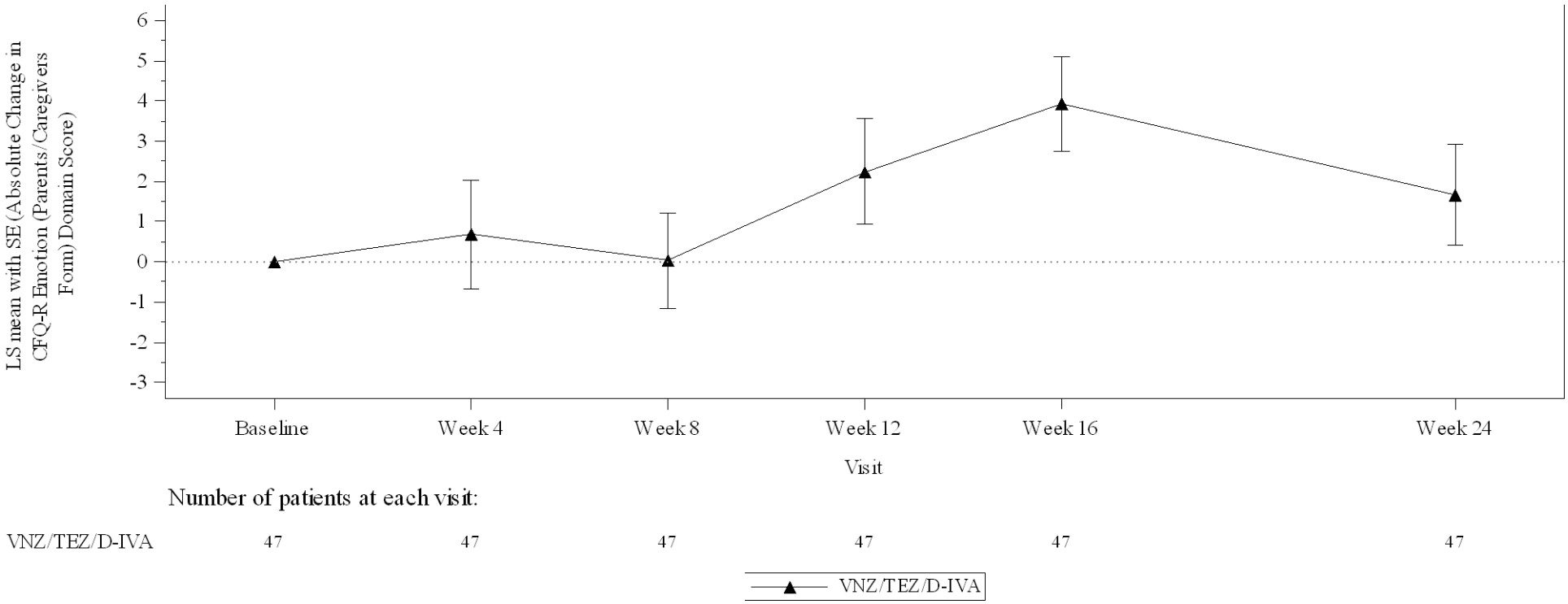

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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

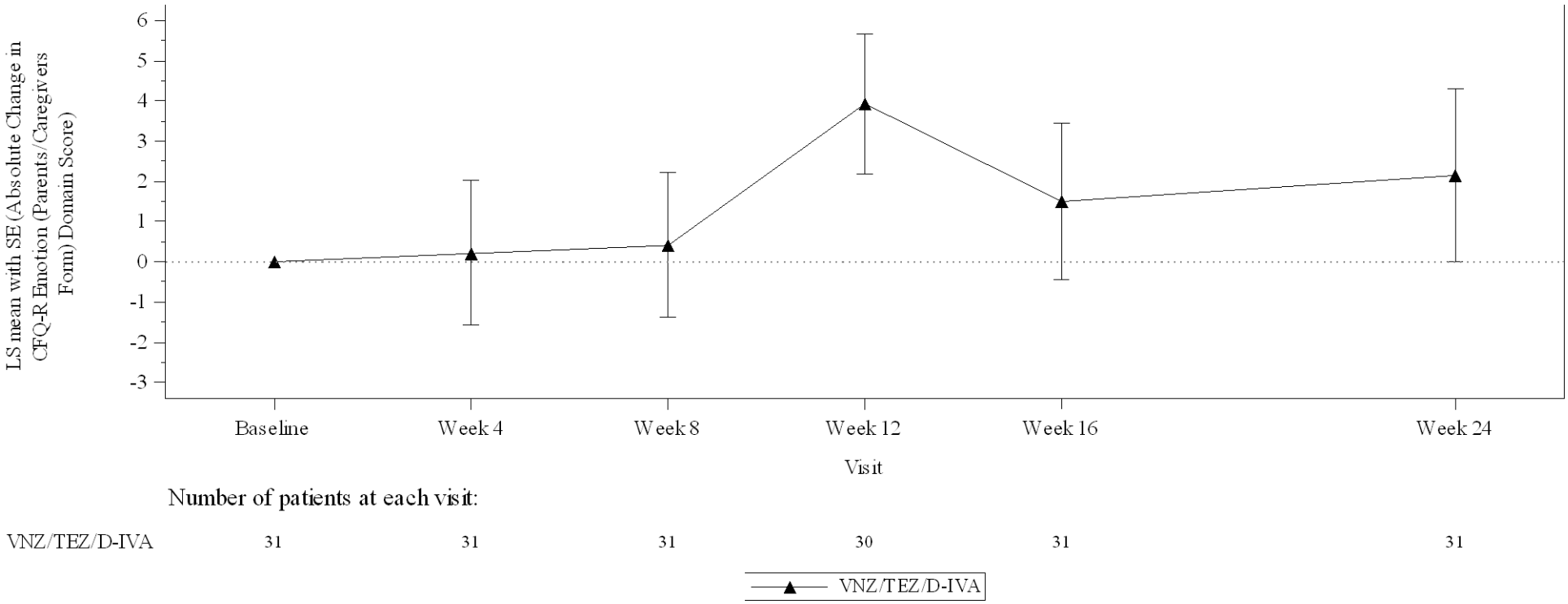

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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

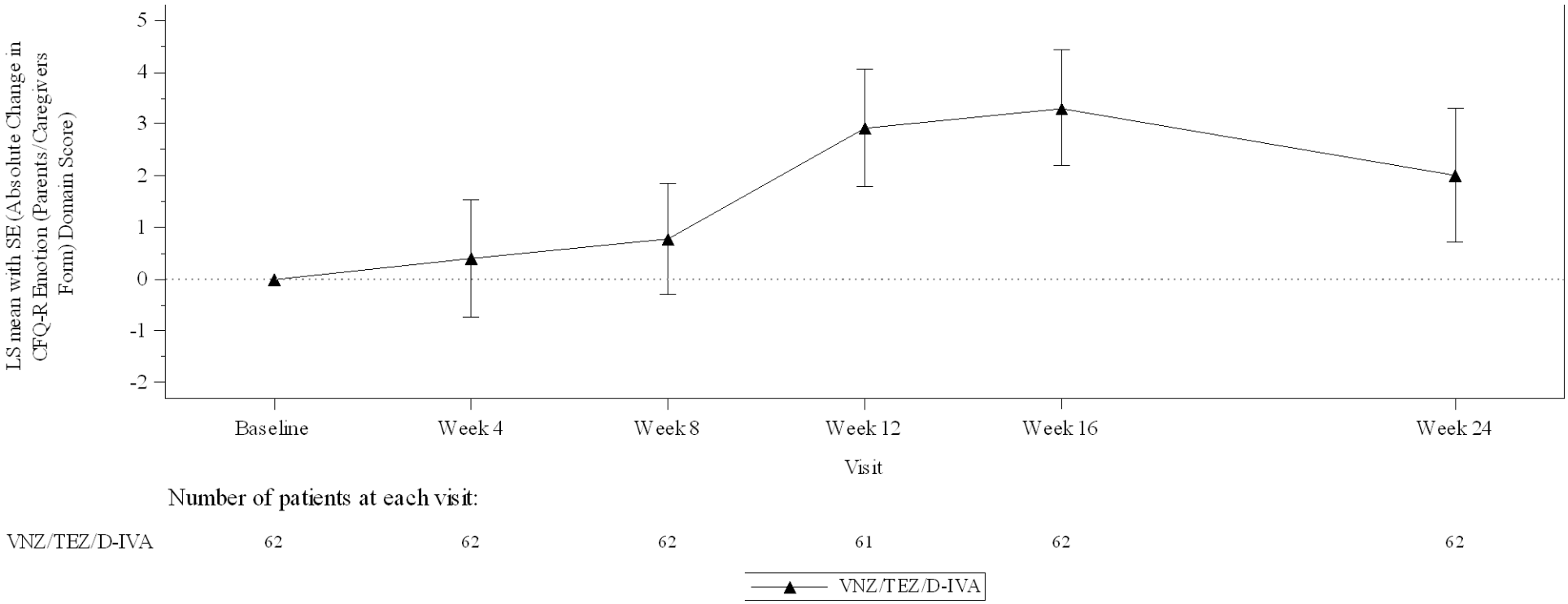

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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

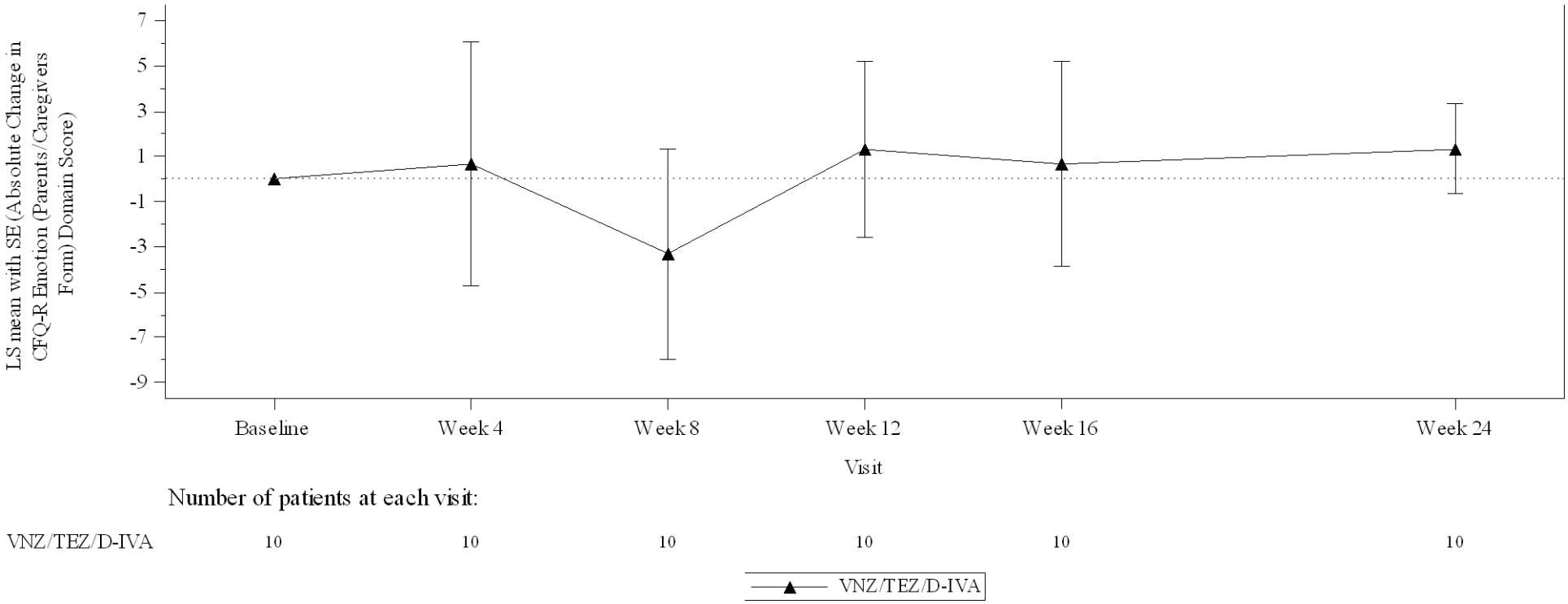

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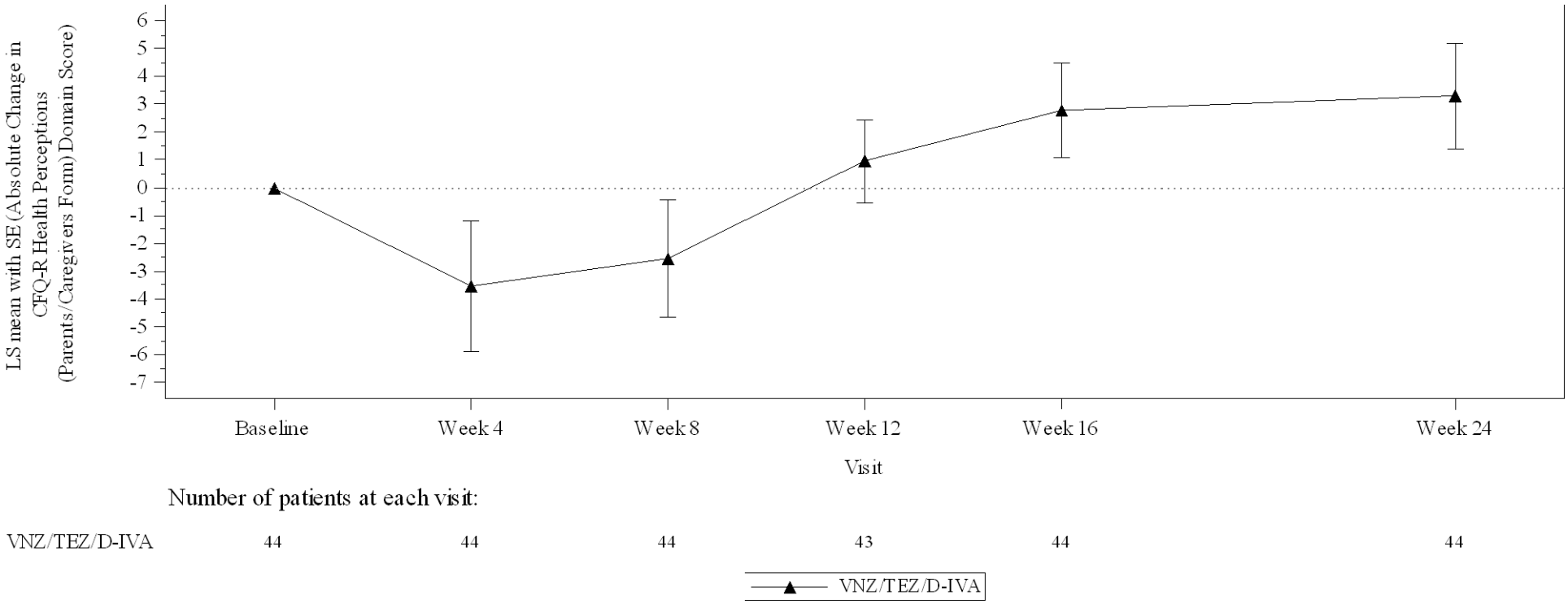
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male



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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

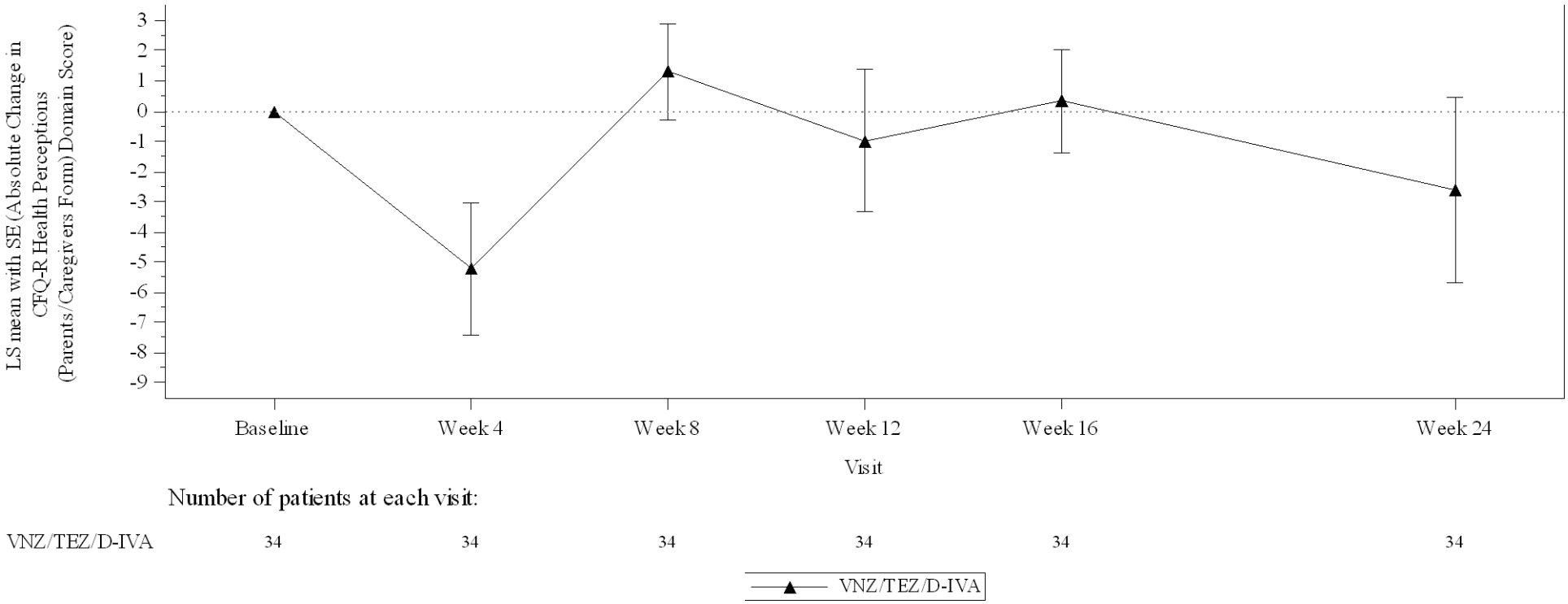

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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

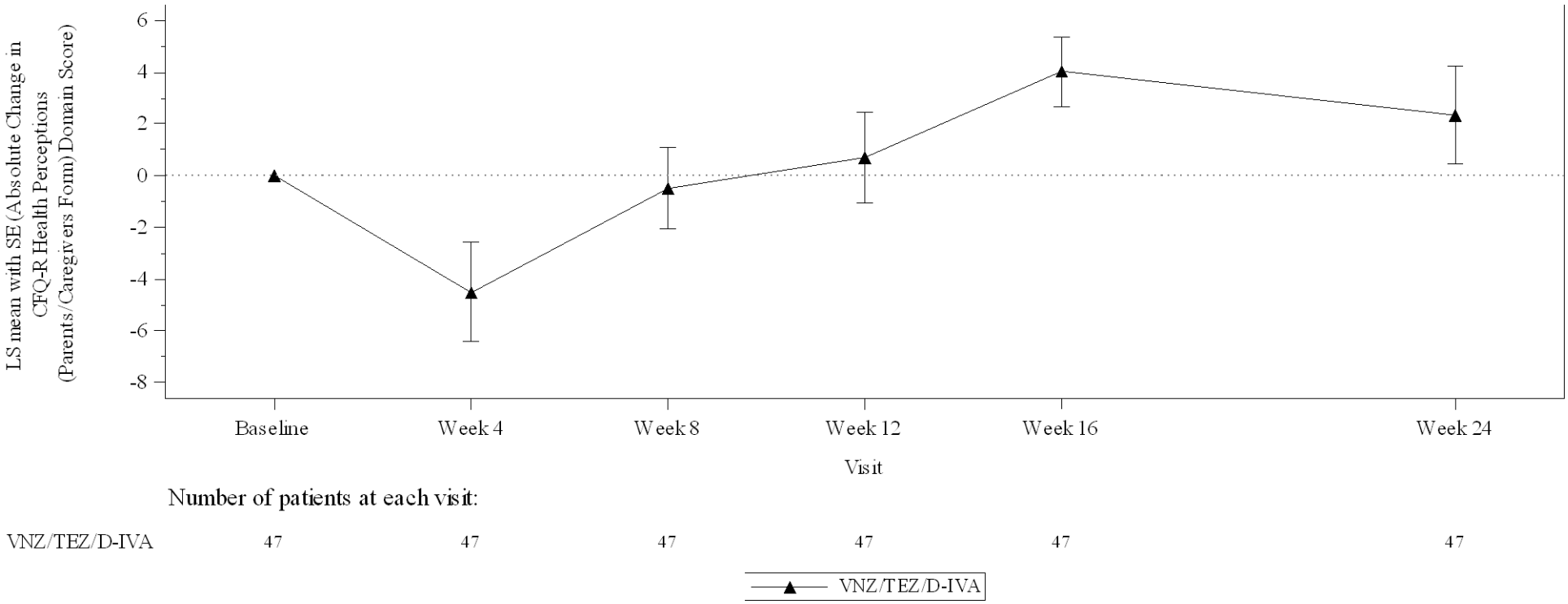

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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

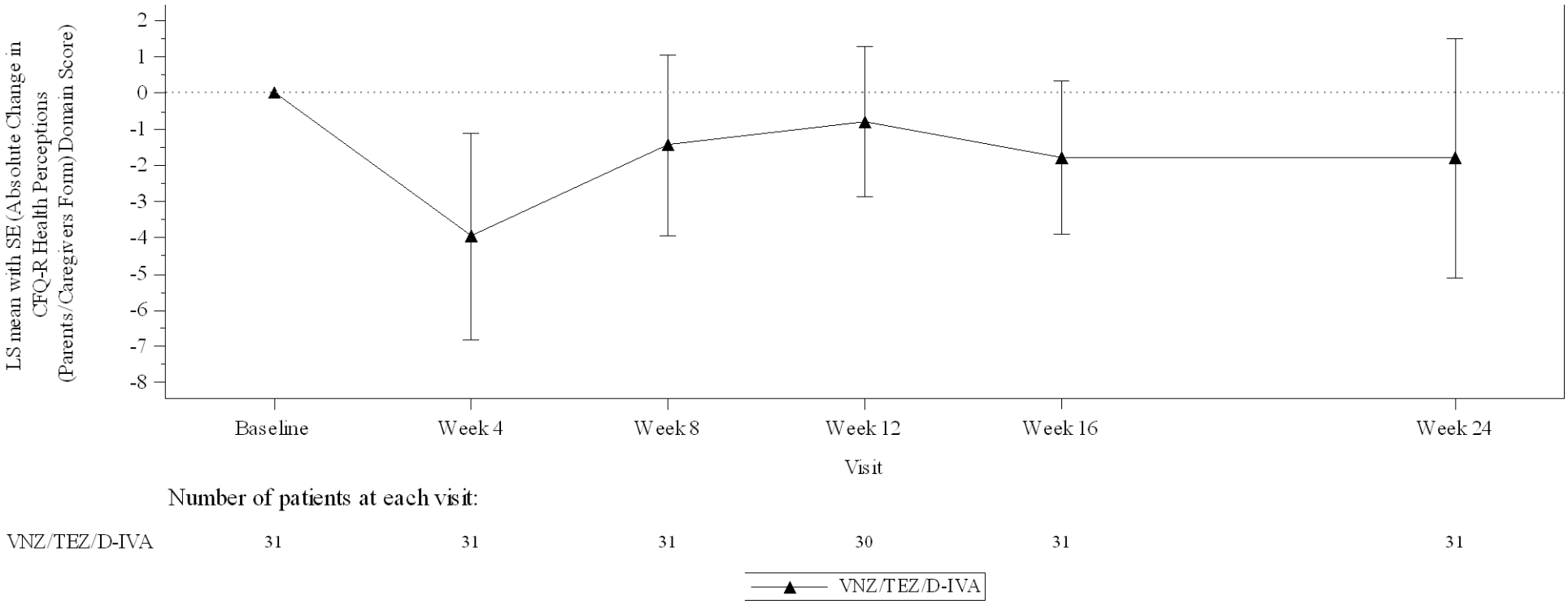

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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

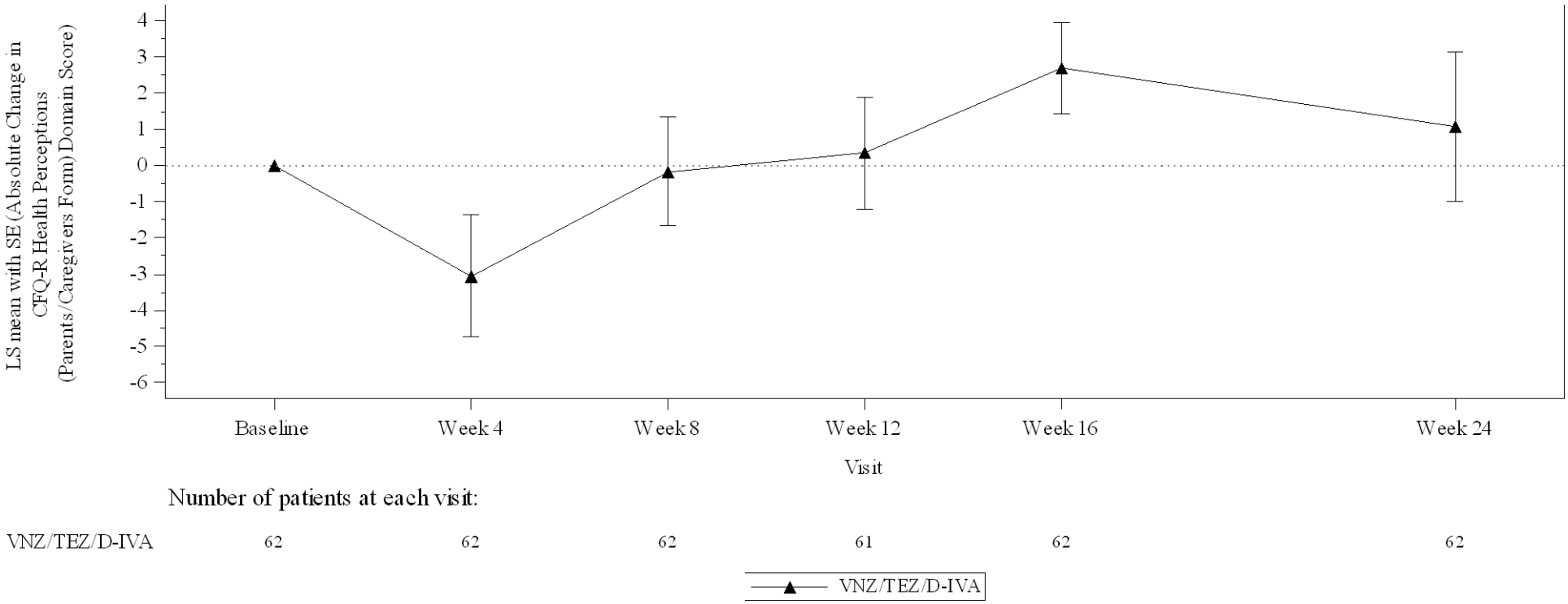

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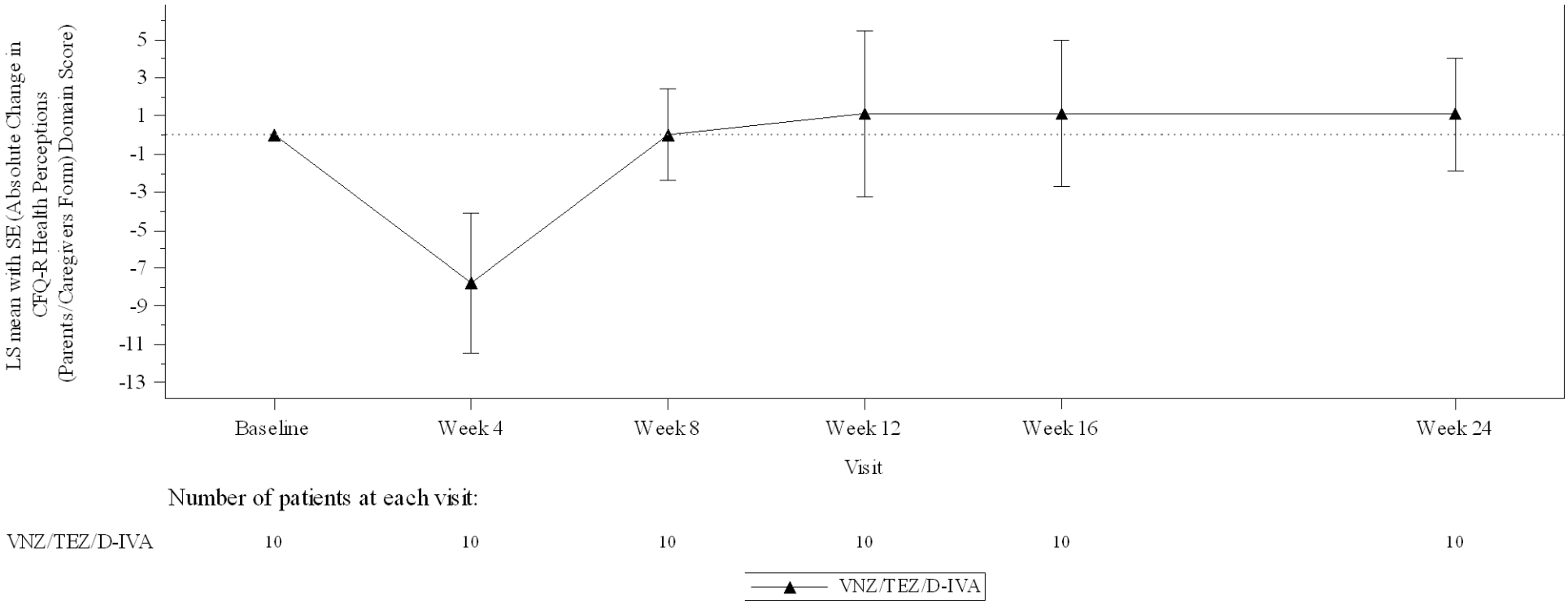
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5



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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Sex = Male

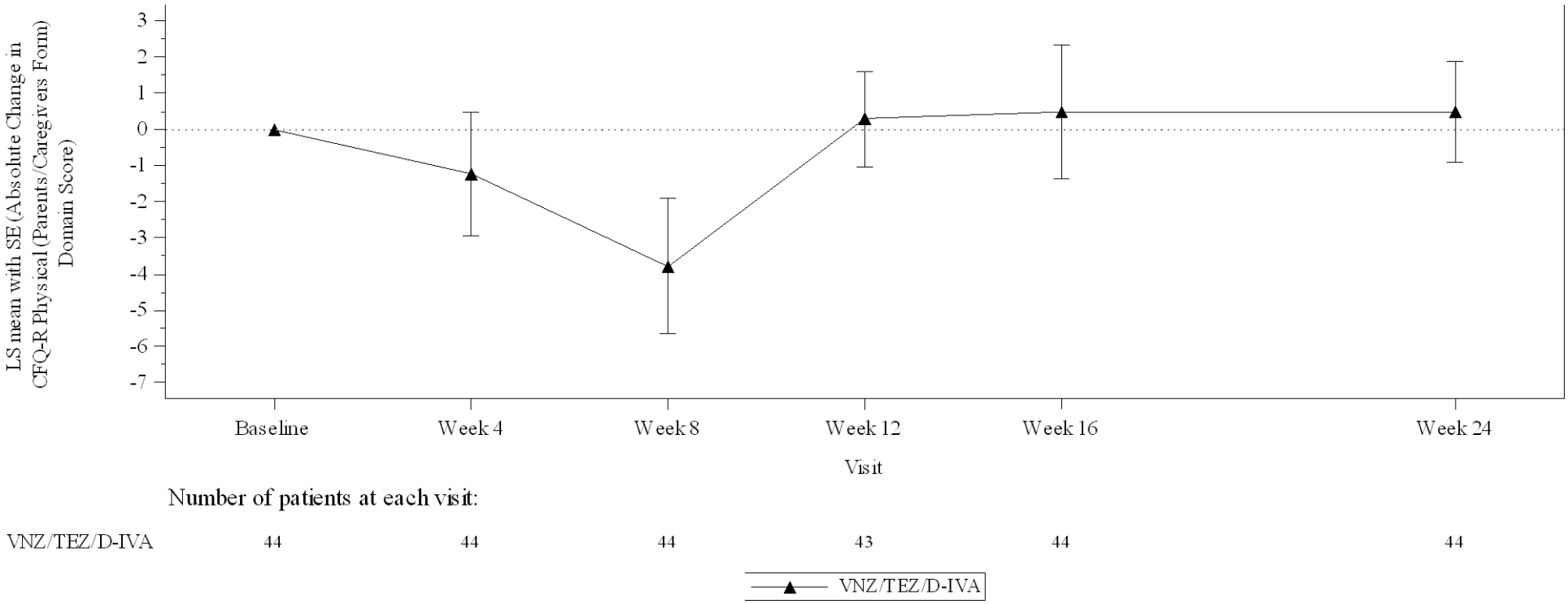

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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Sex = Female

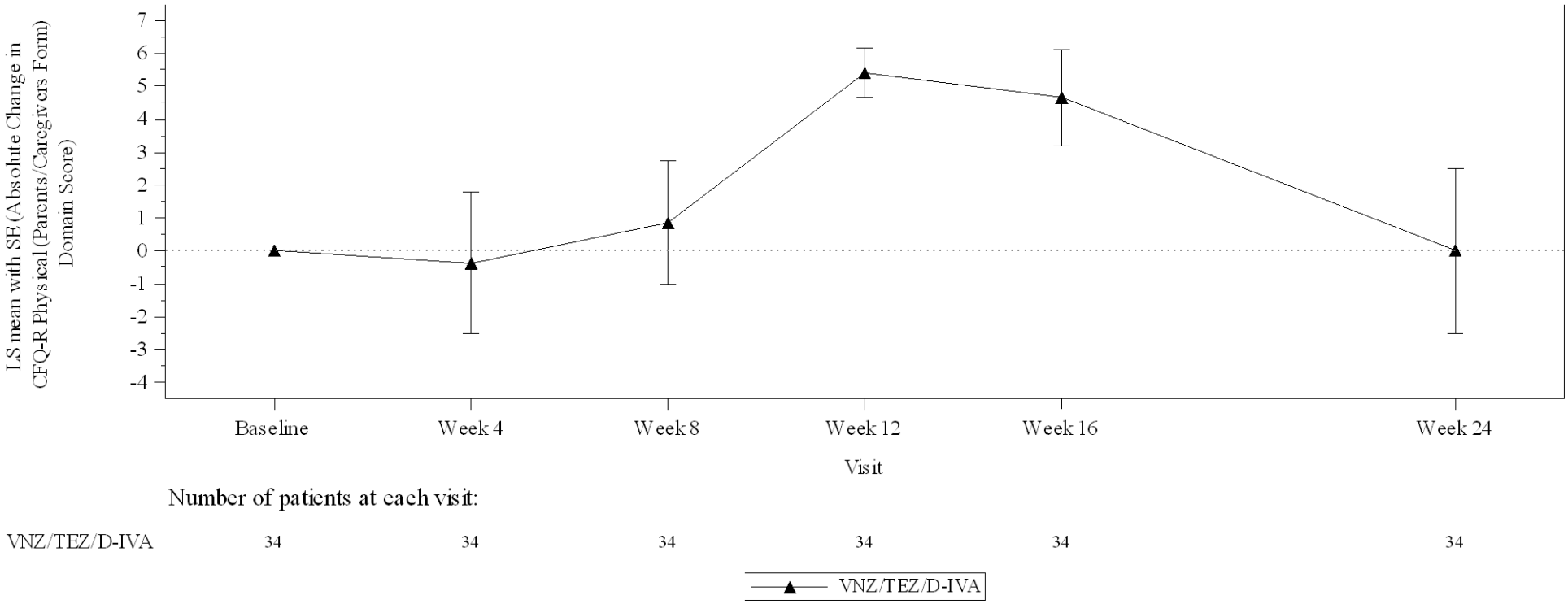

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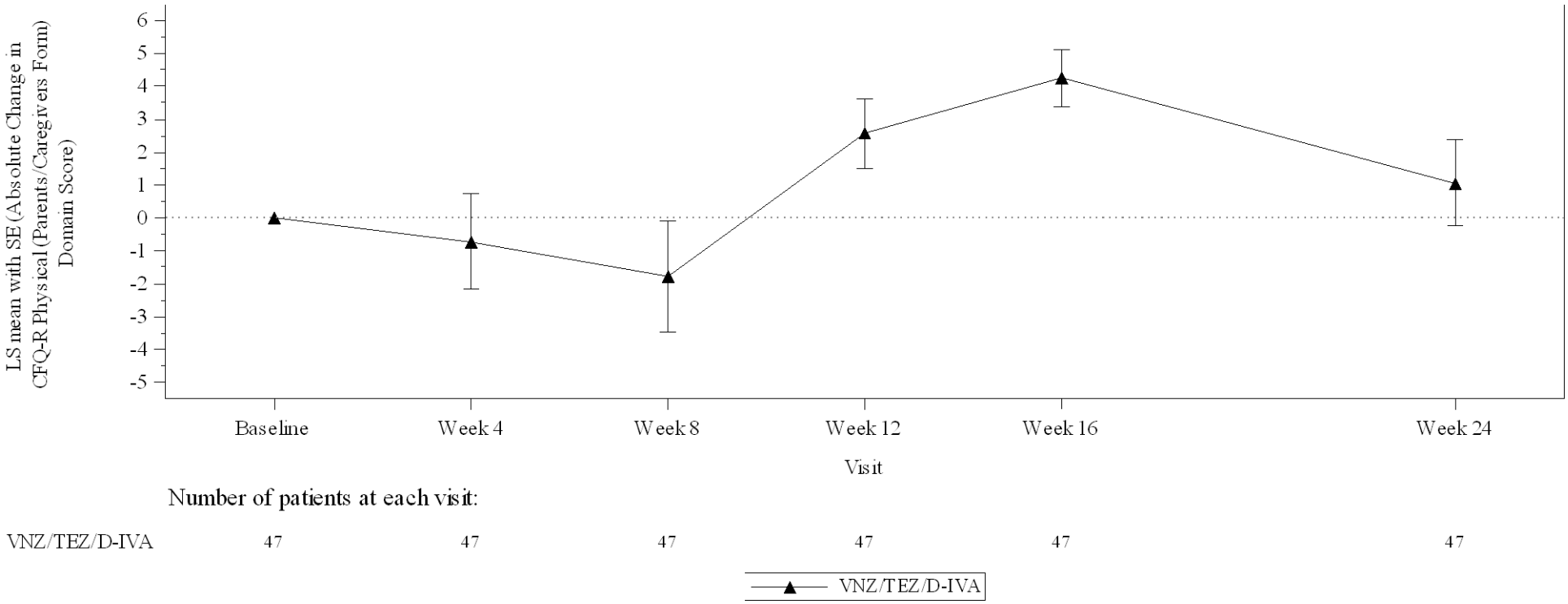
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Region = North America



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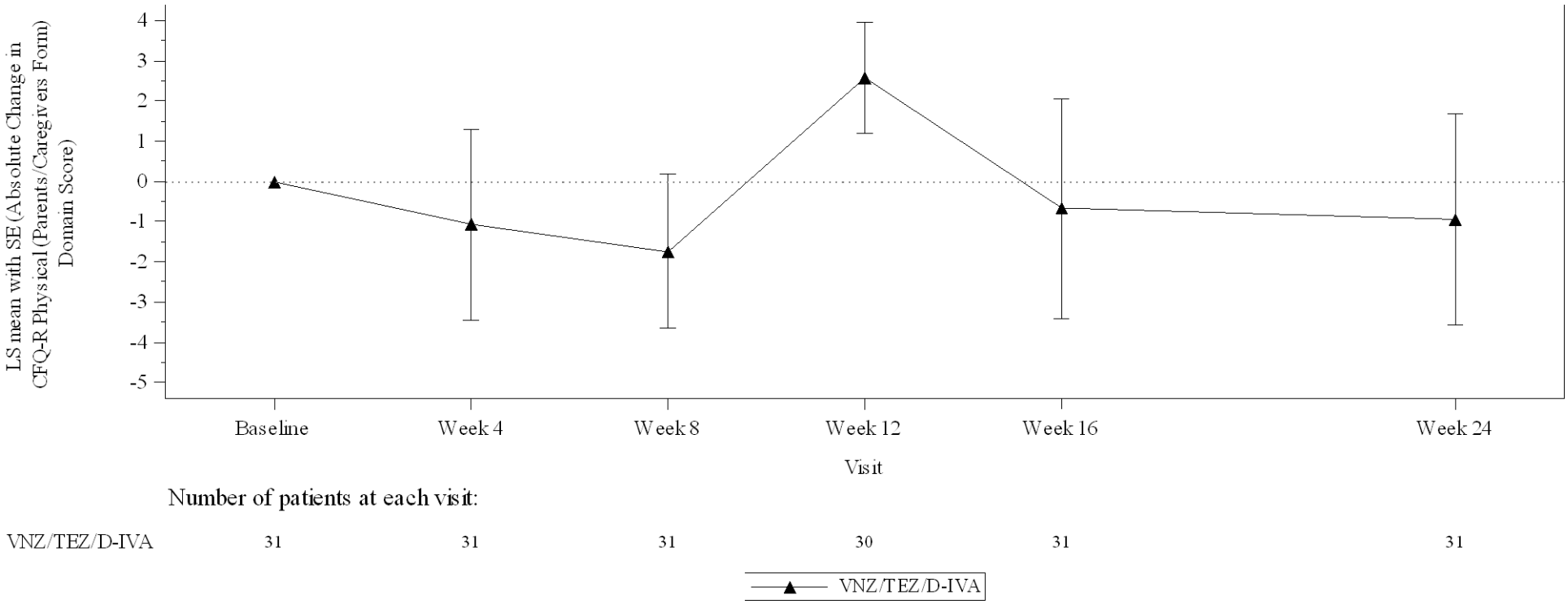
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

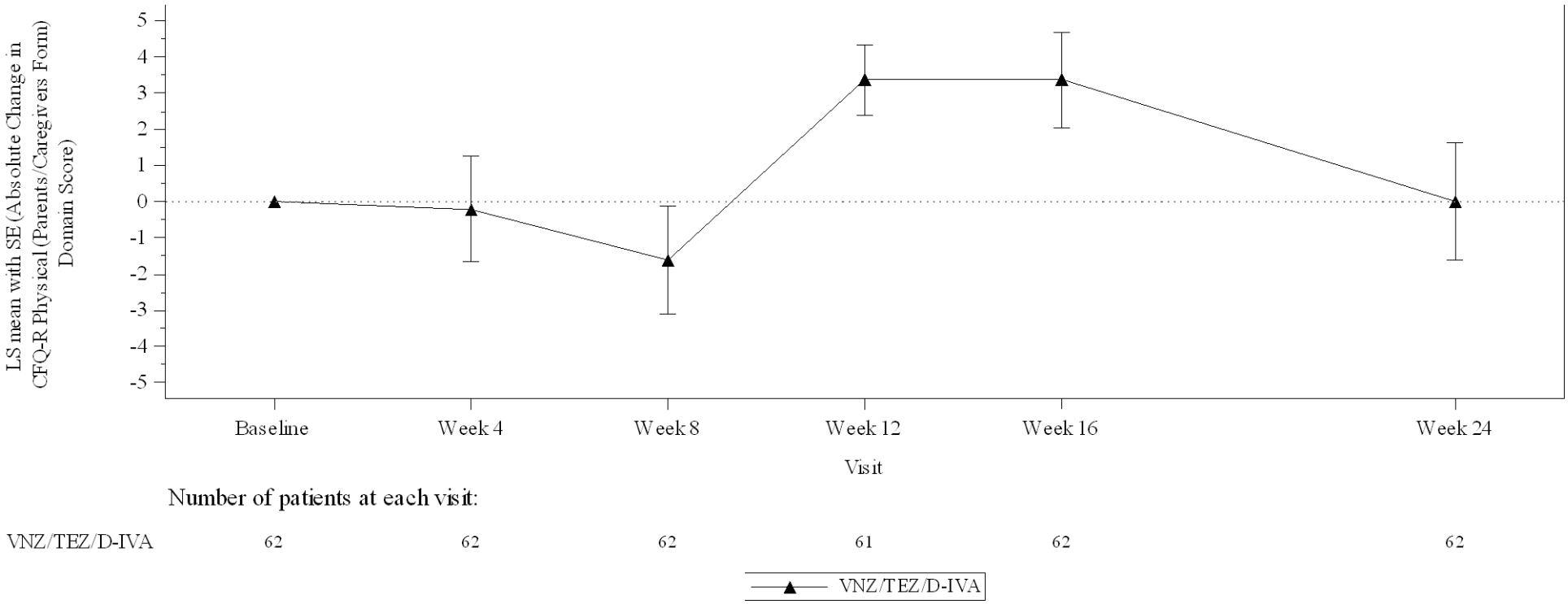
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

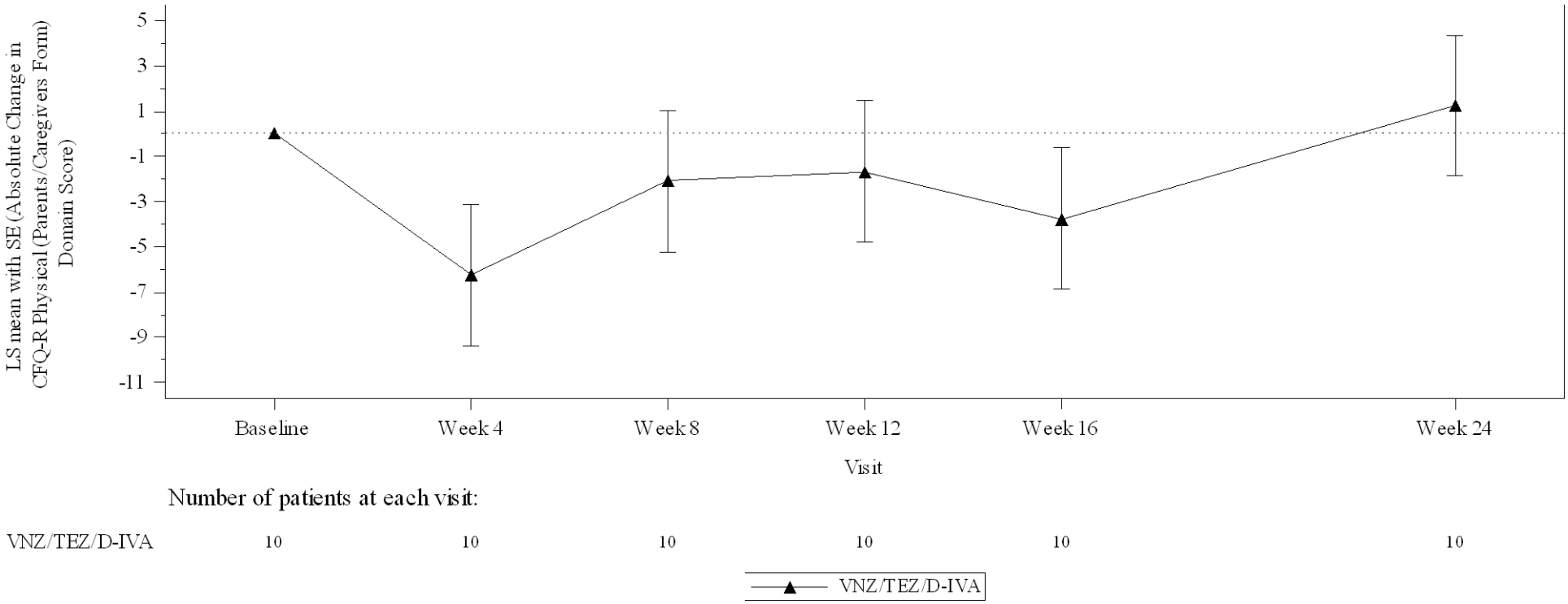
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

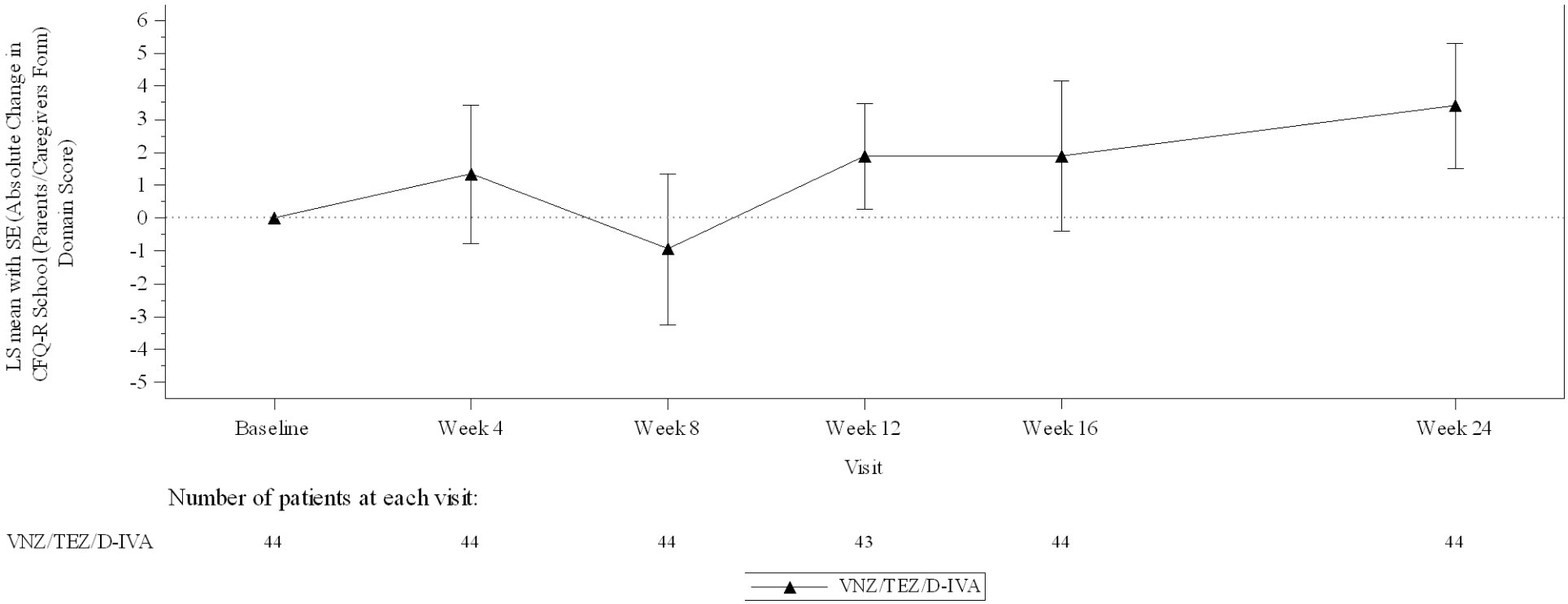
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

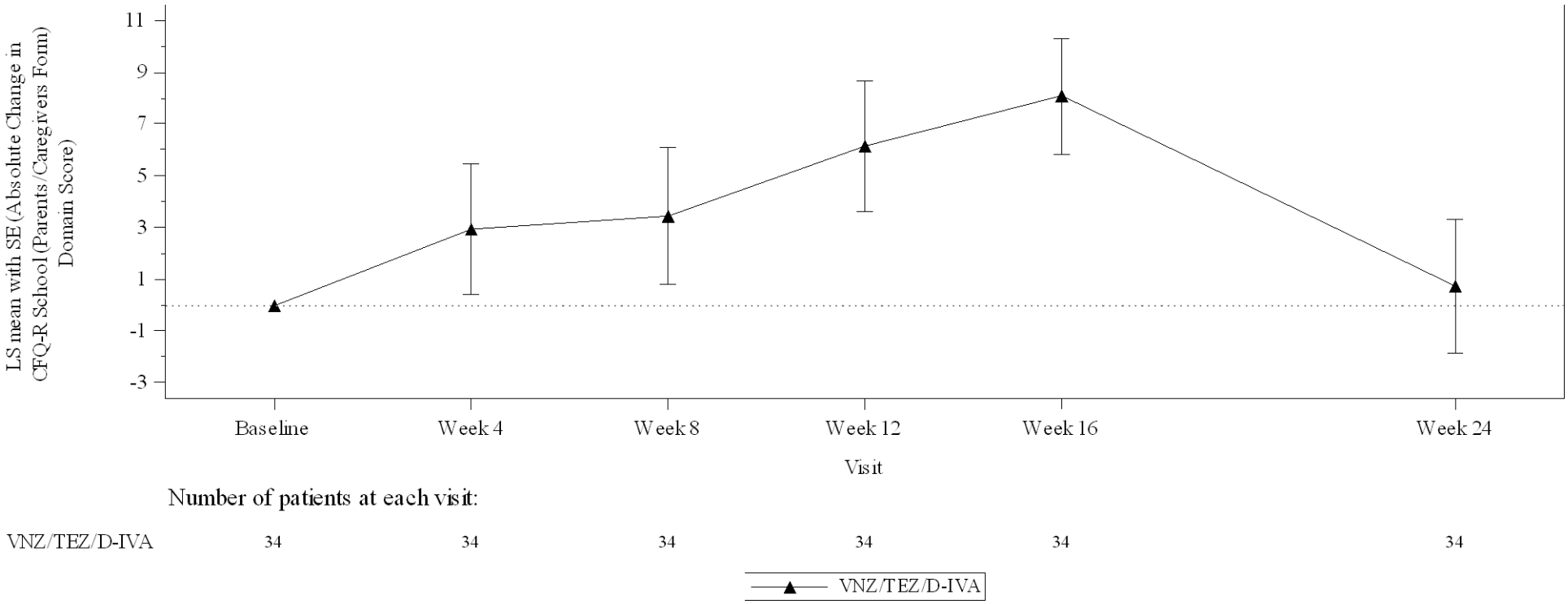
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

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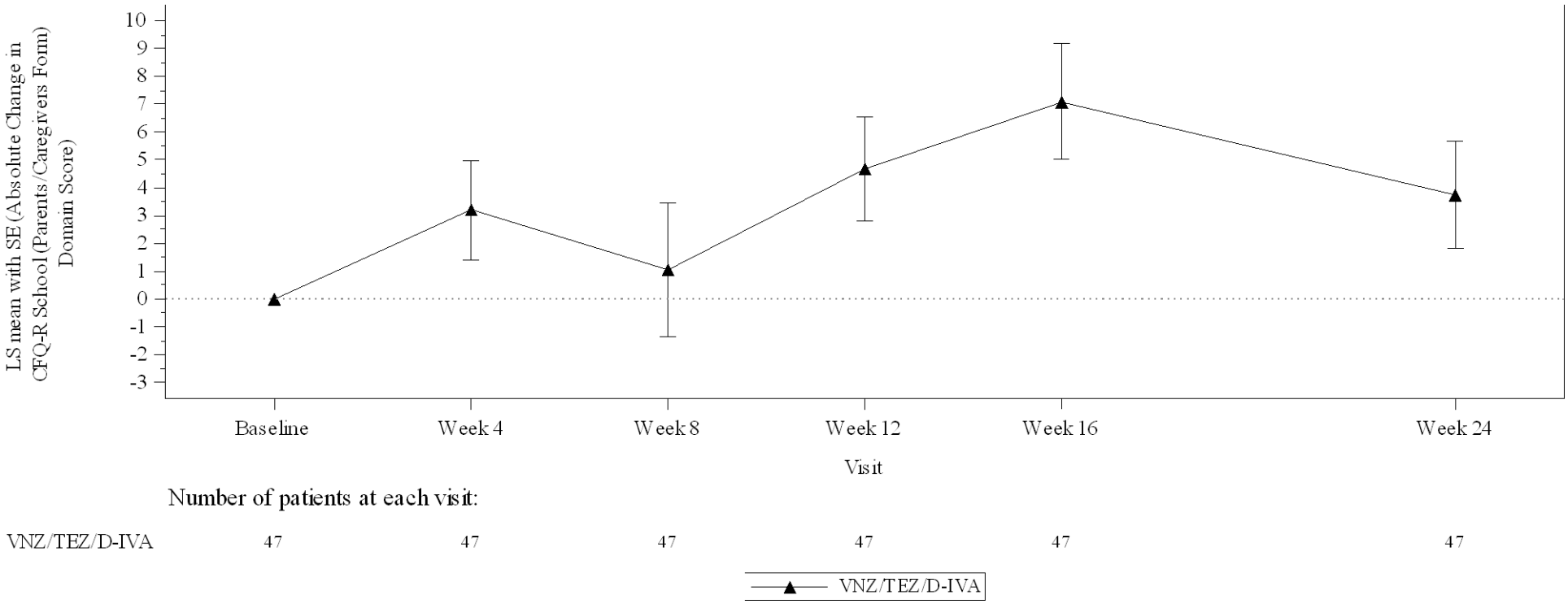
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Region = North America



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- Baseline is defined as the pre-dose Day 1 value.
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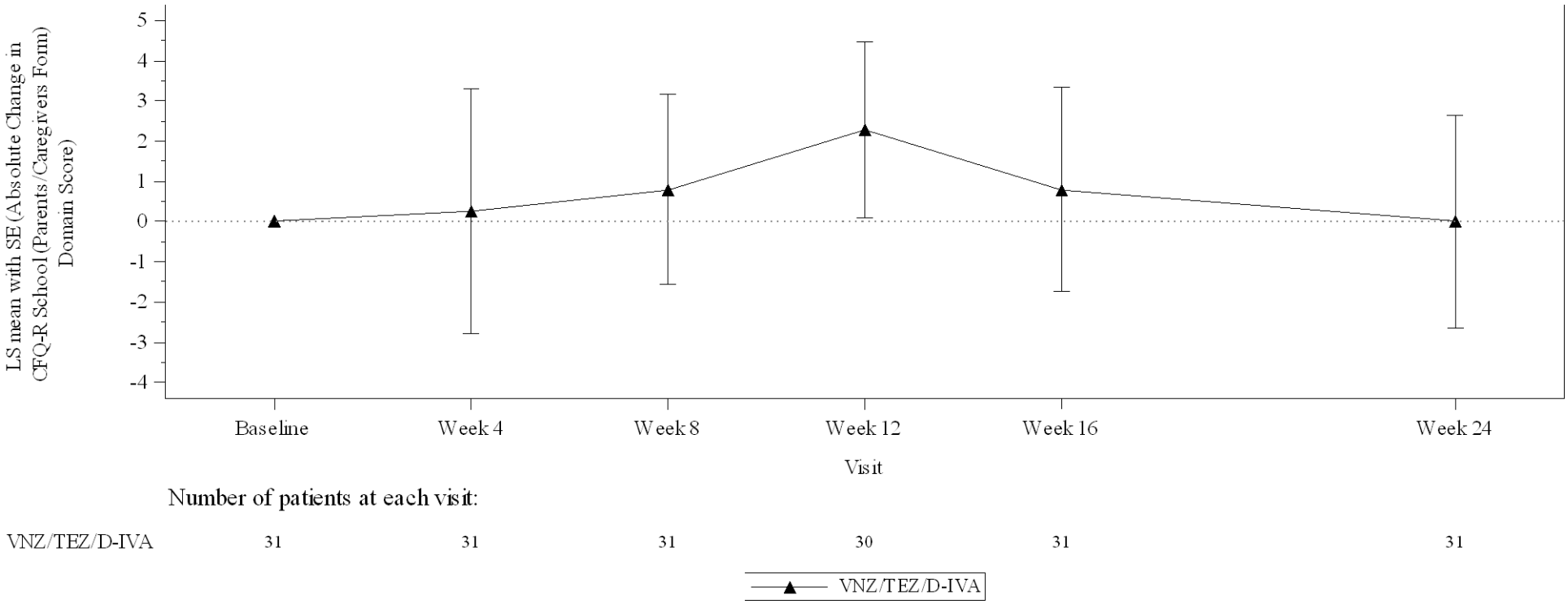
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Region = Rest of World



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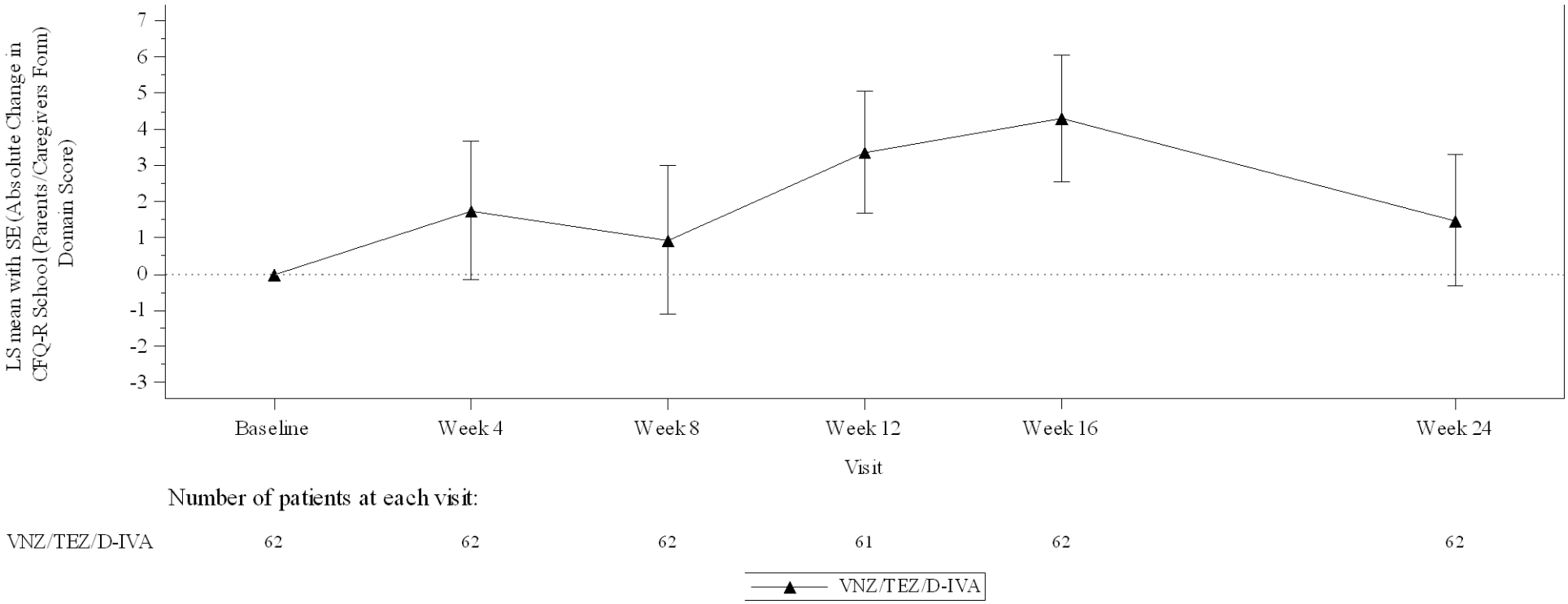
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5



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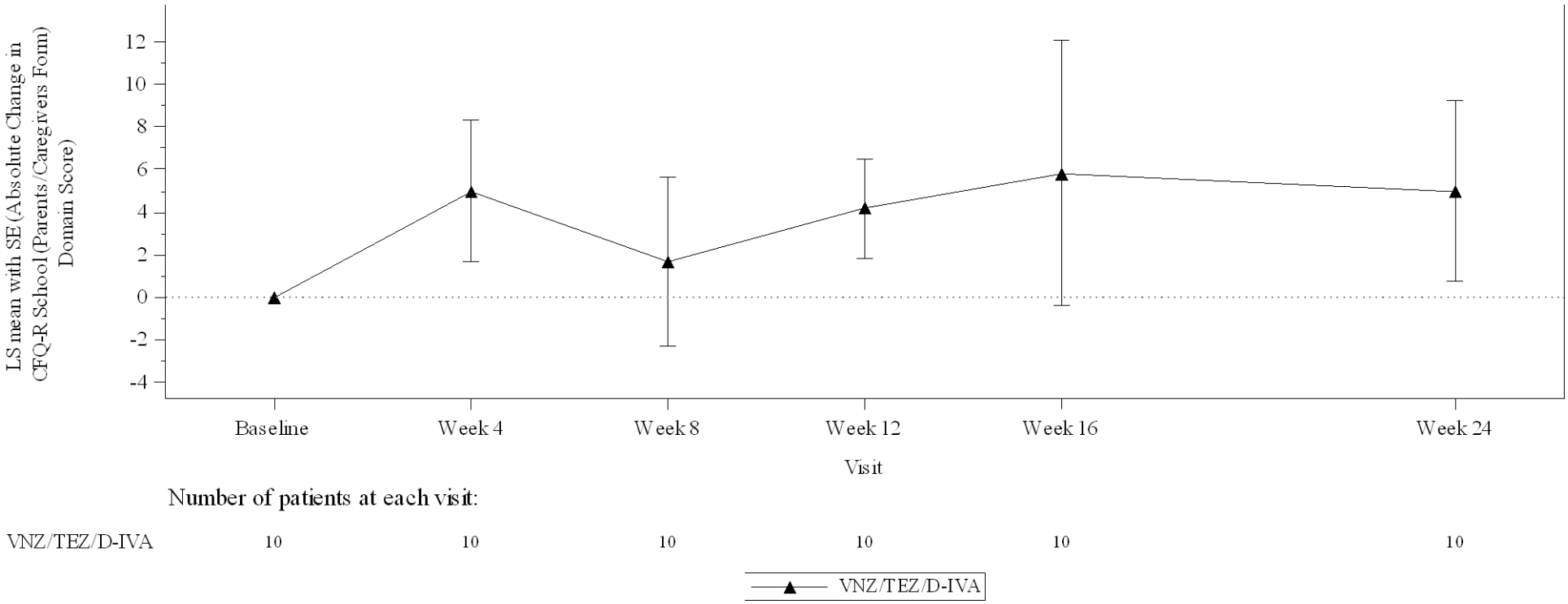
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5



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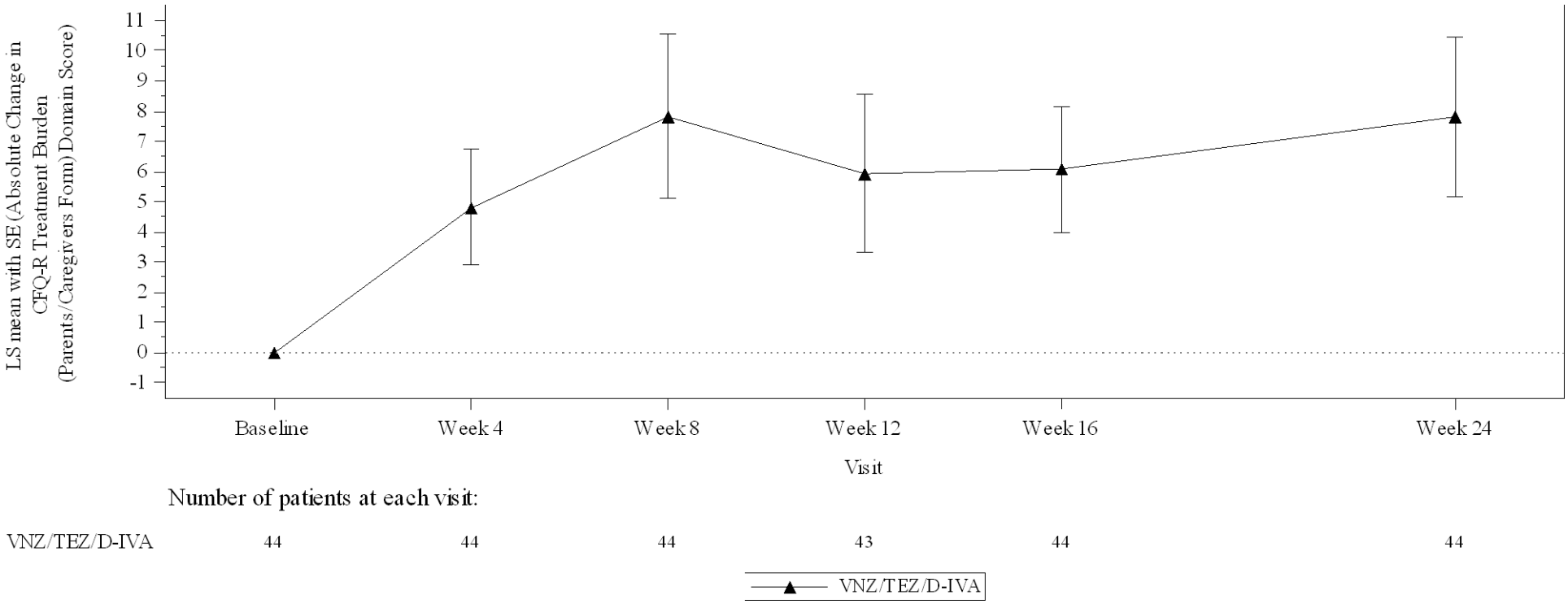
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

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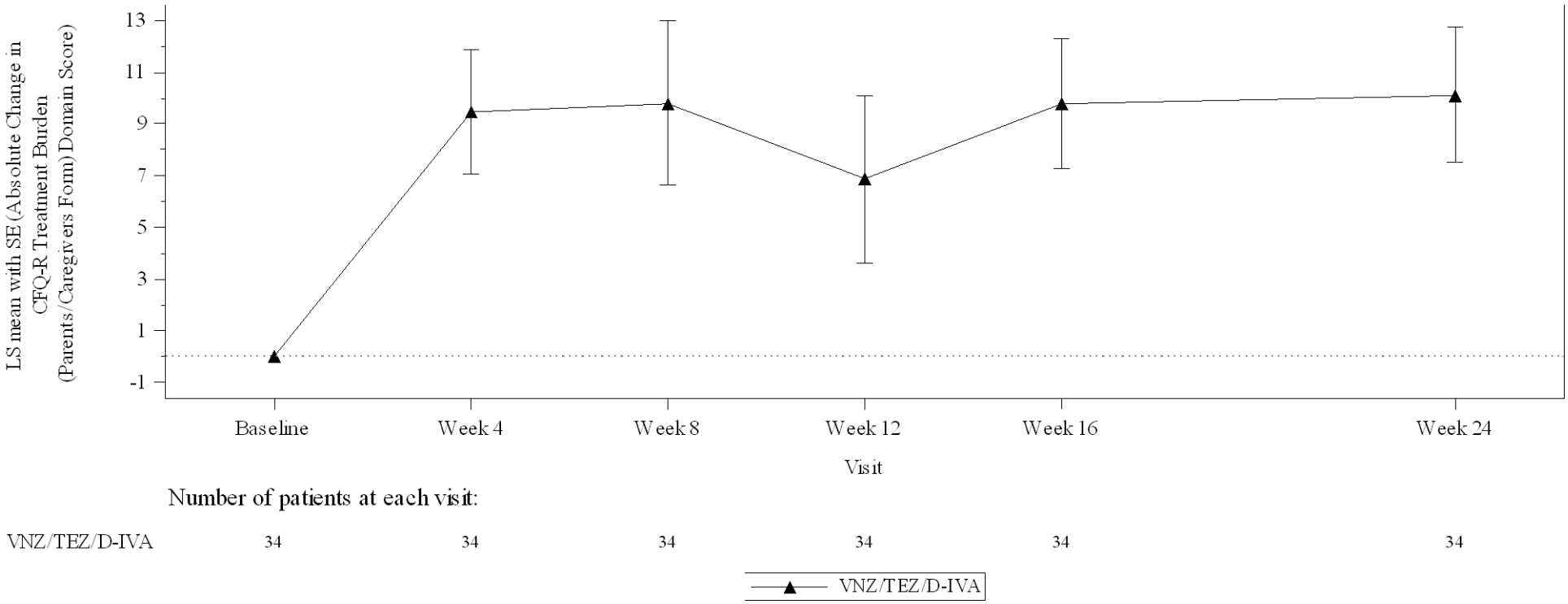
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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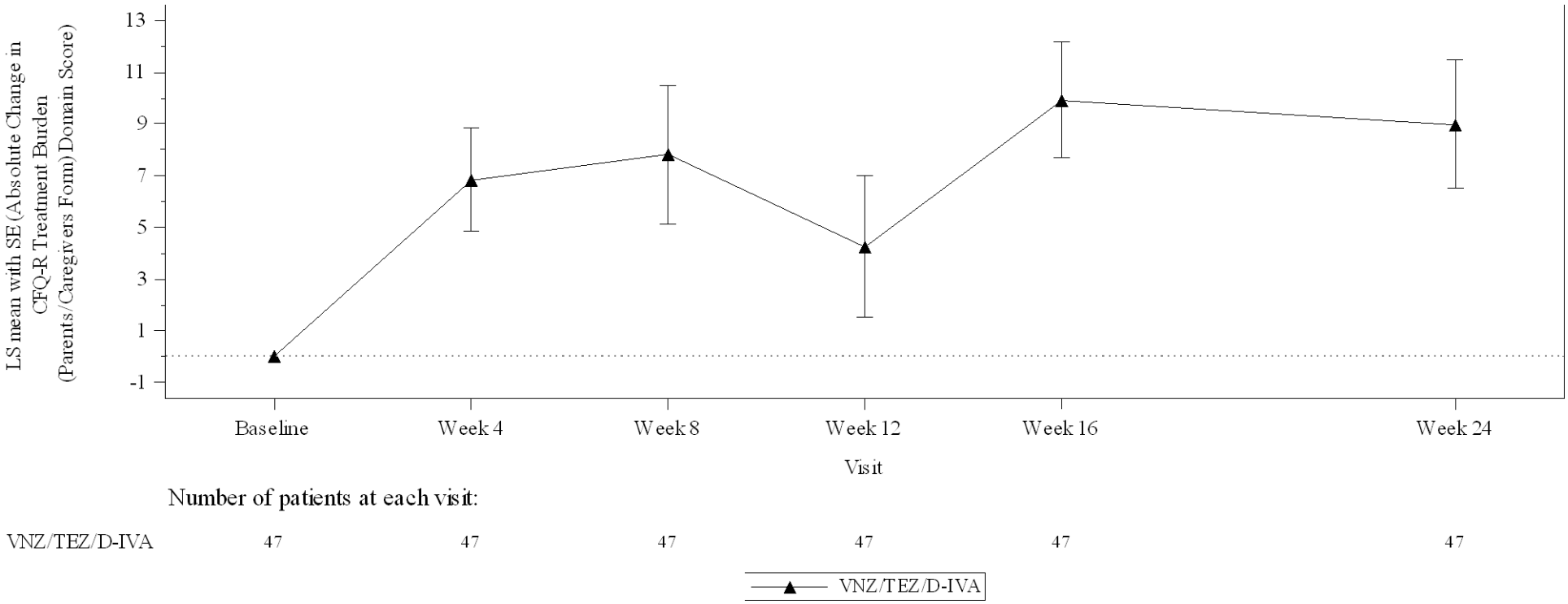
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America



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- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

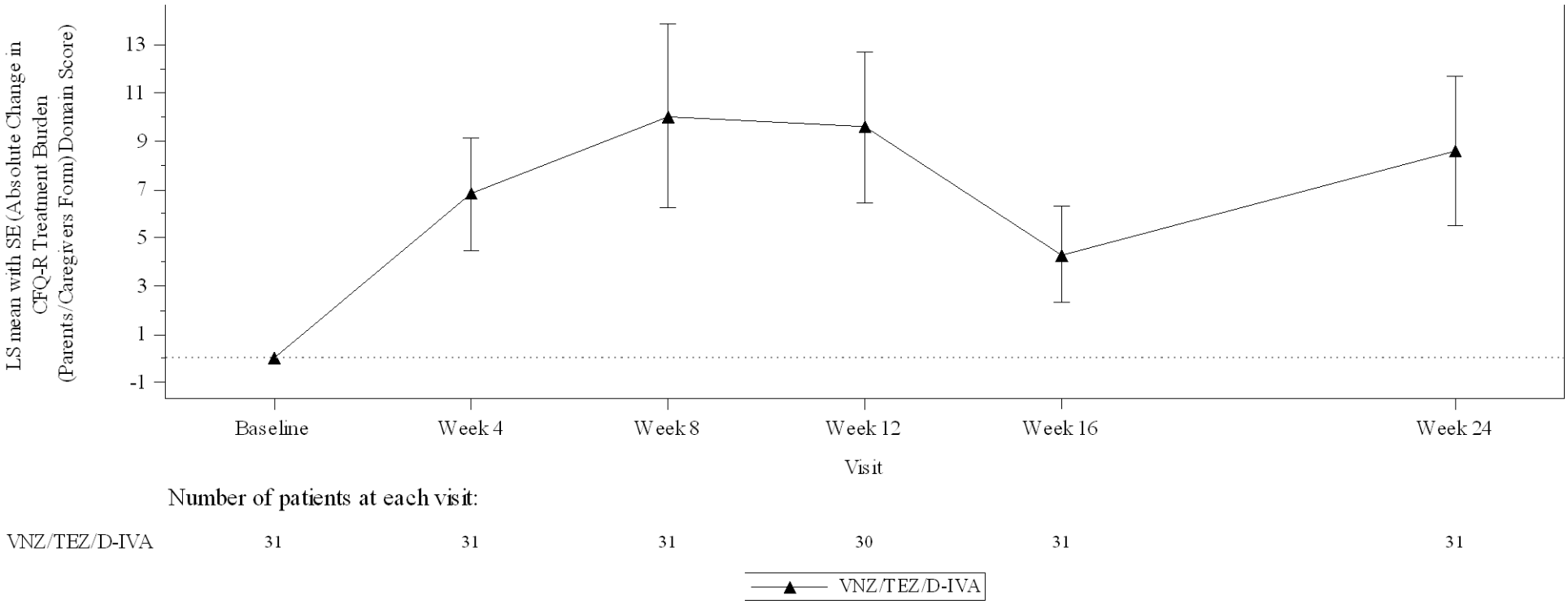

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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

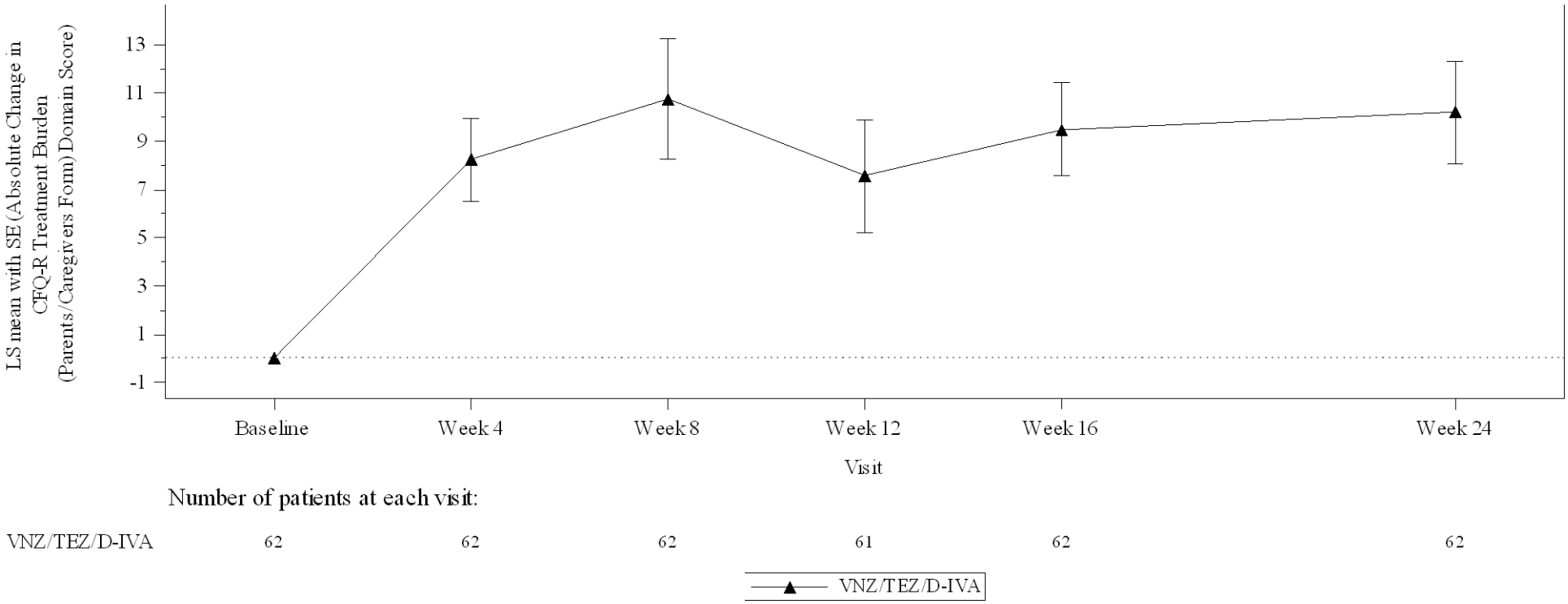

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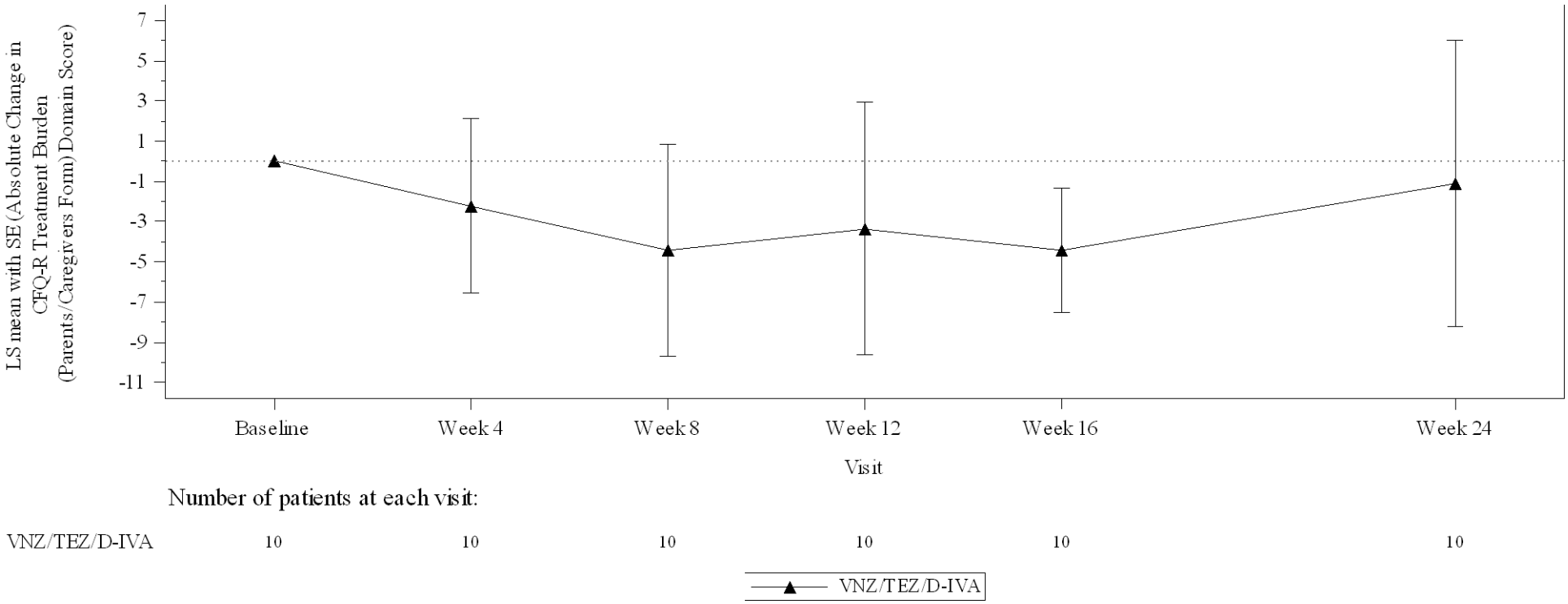
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5



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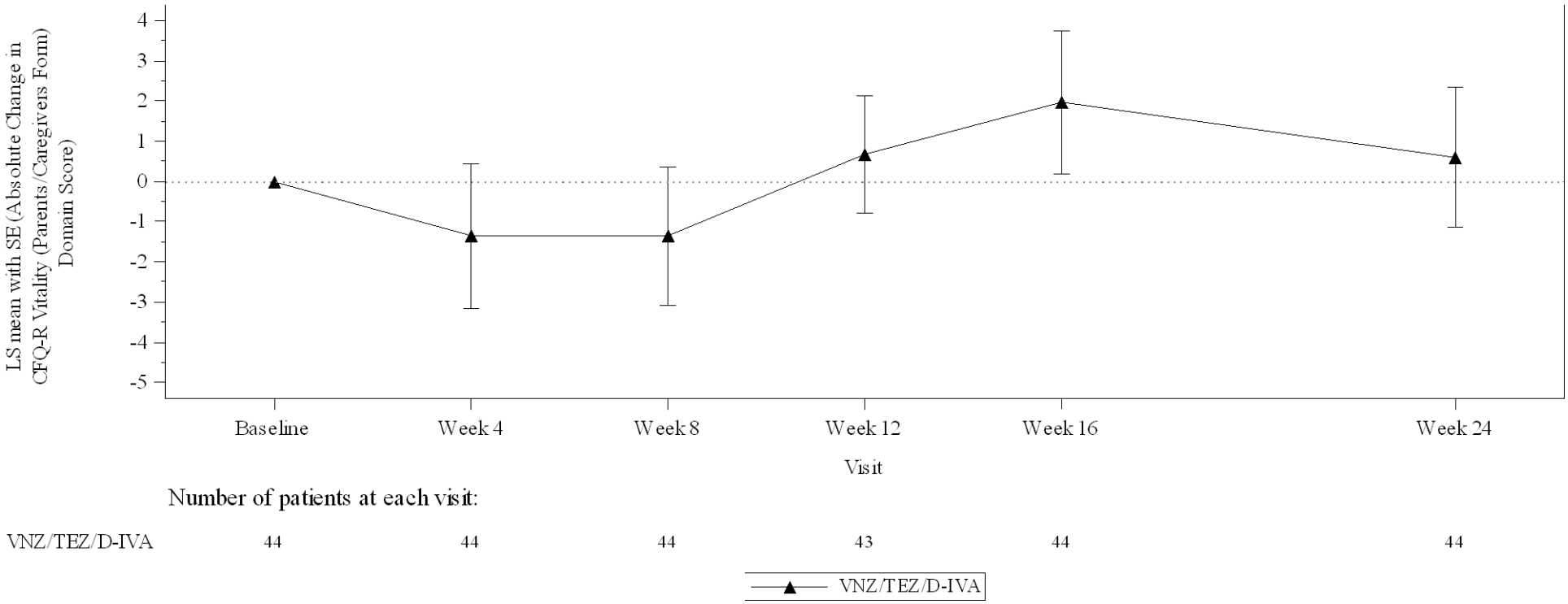
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Sex = Male



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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Sex = Female

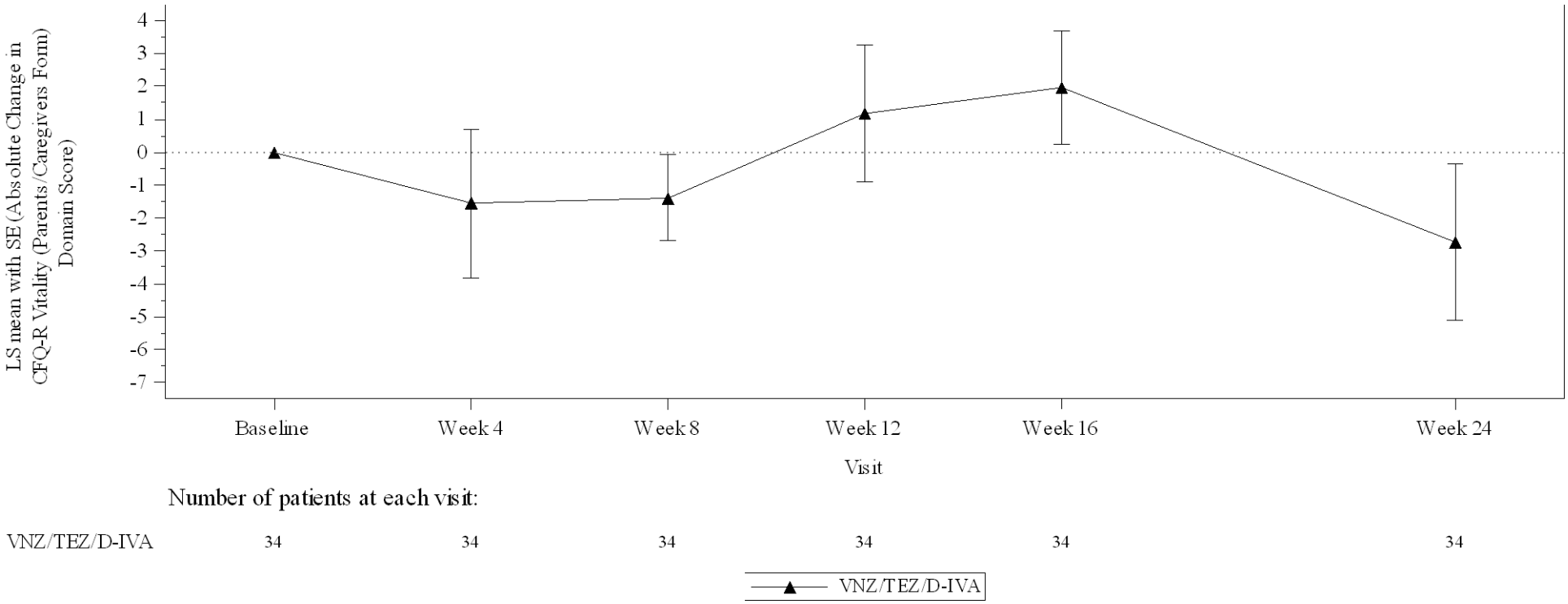

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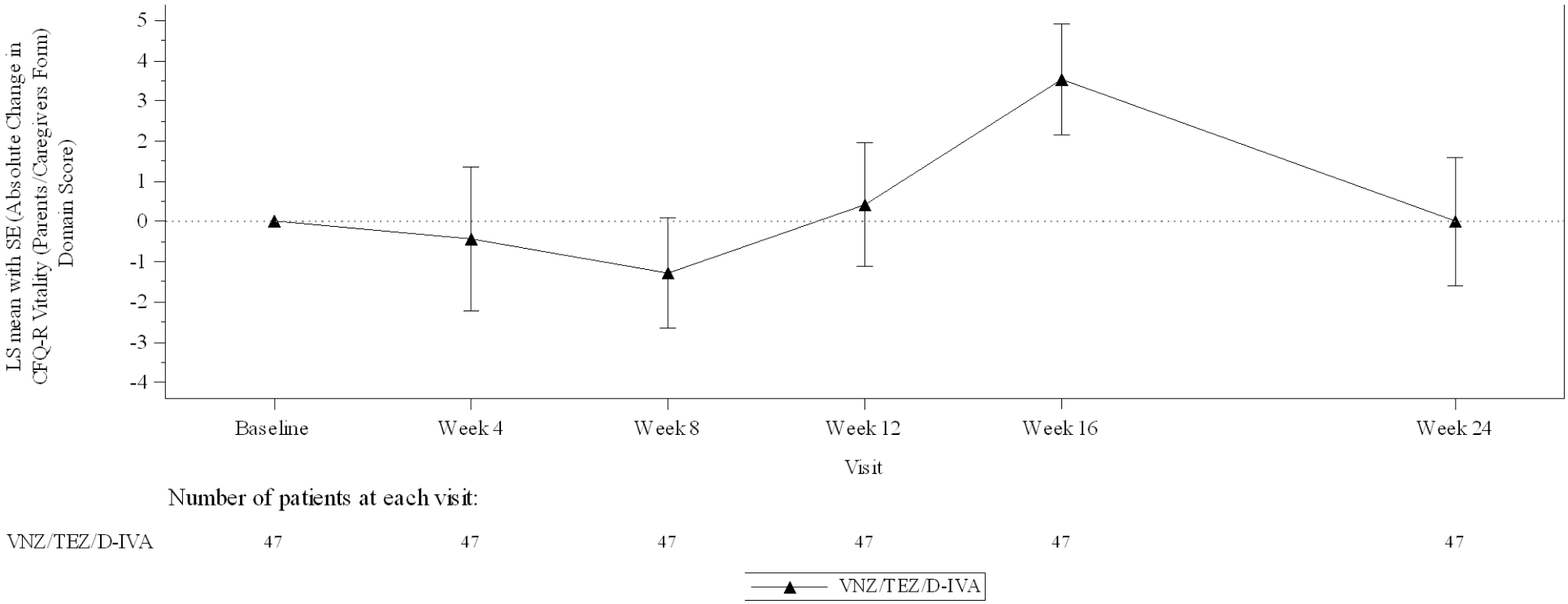
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Region = North America



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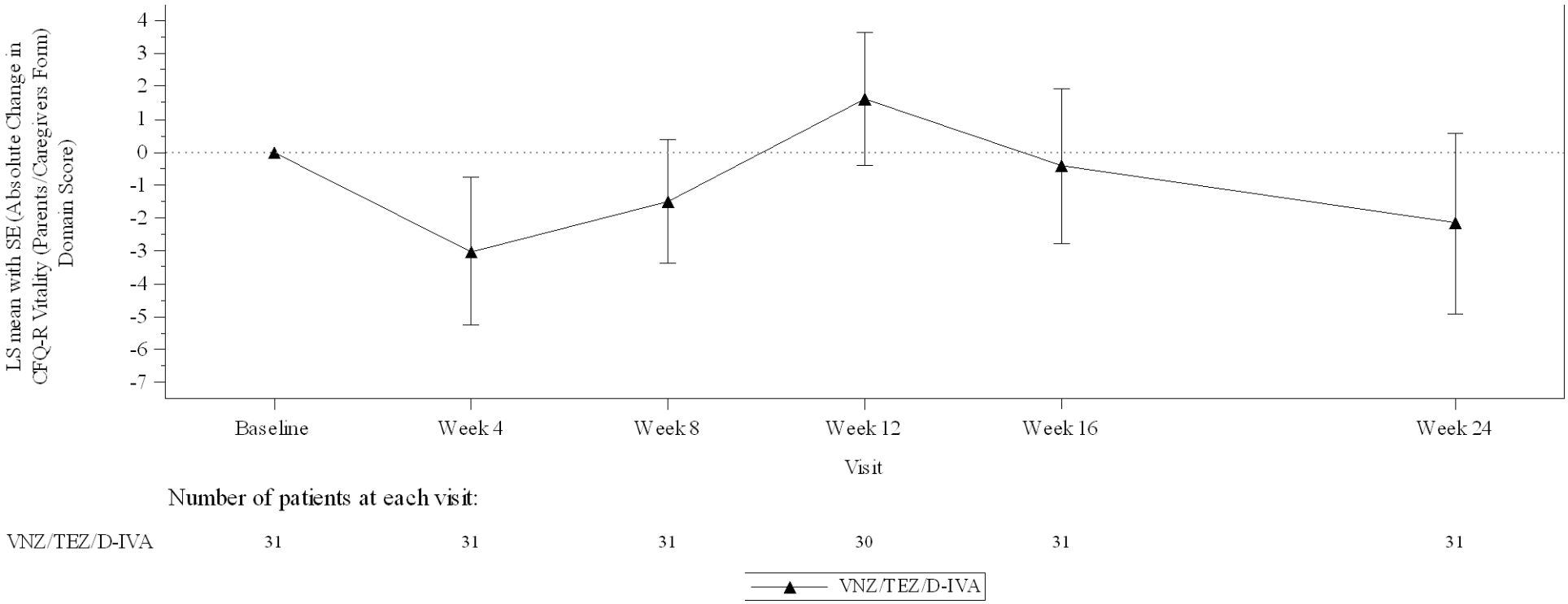
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World



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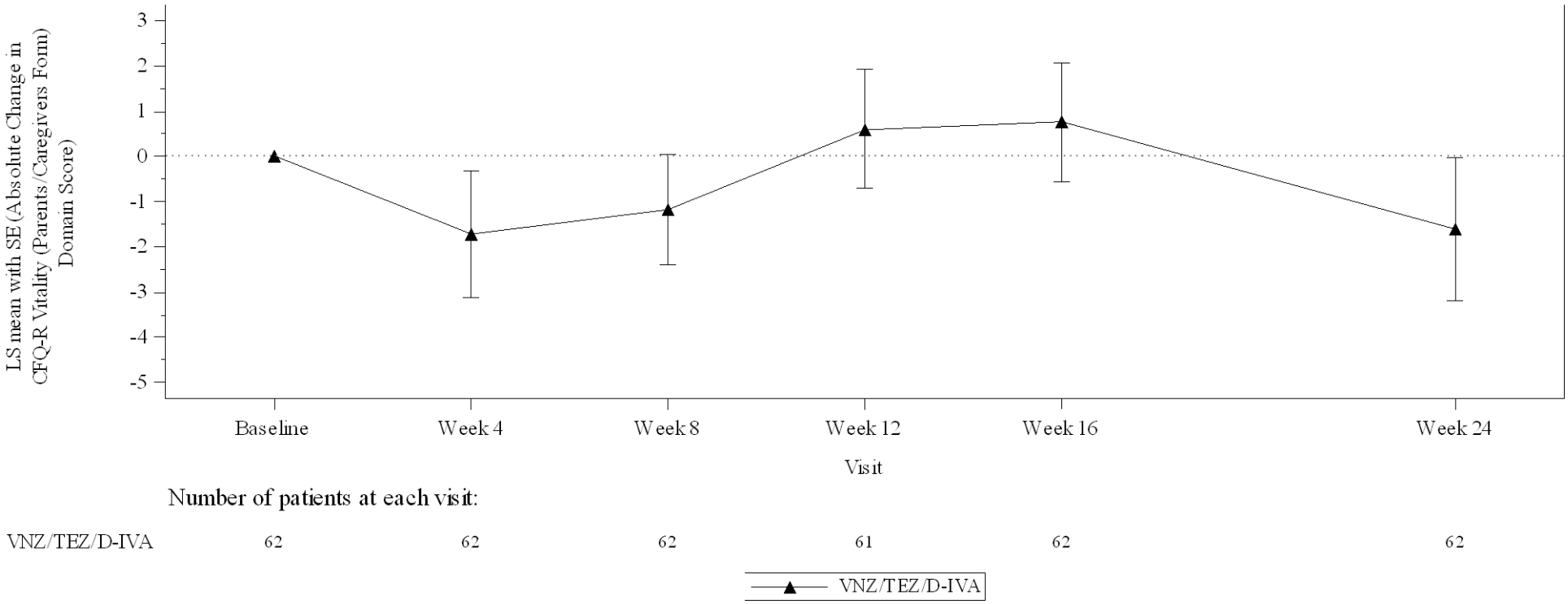
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5



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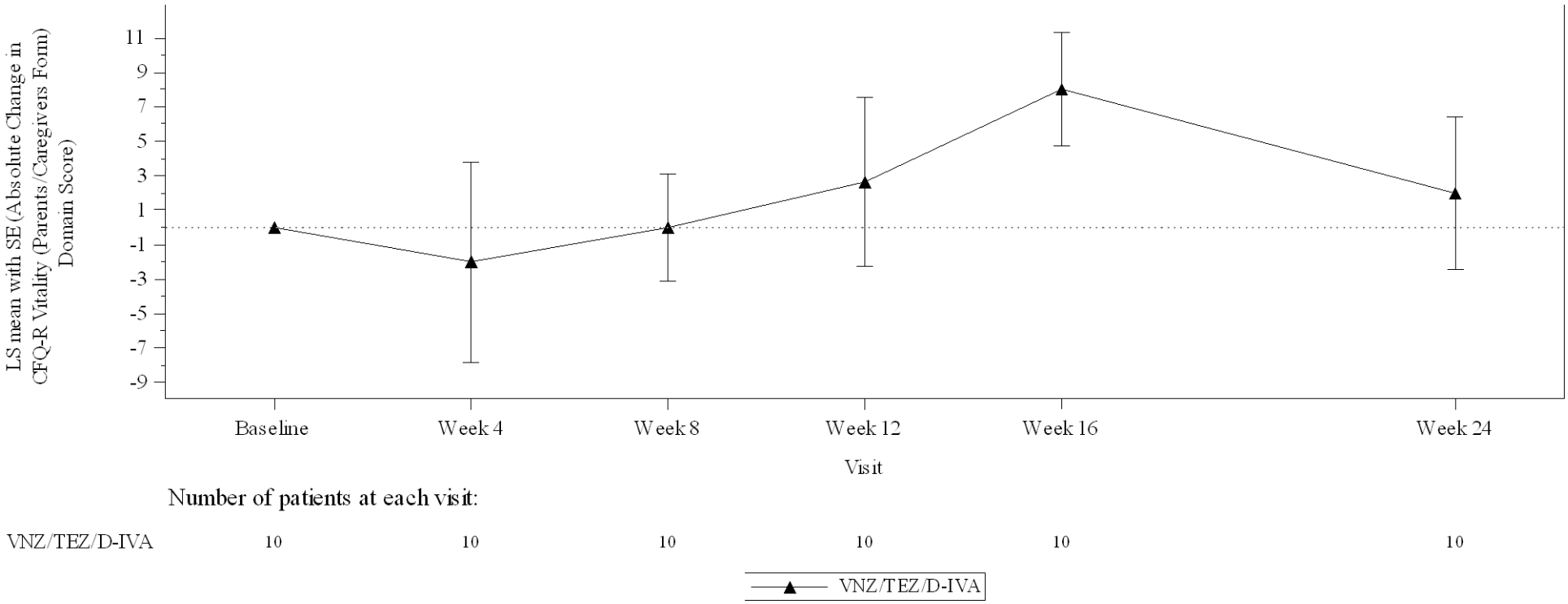
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

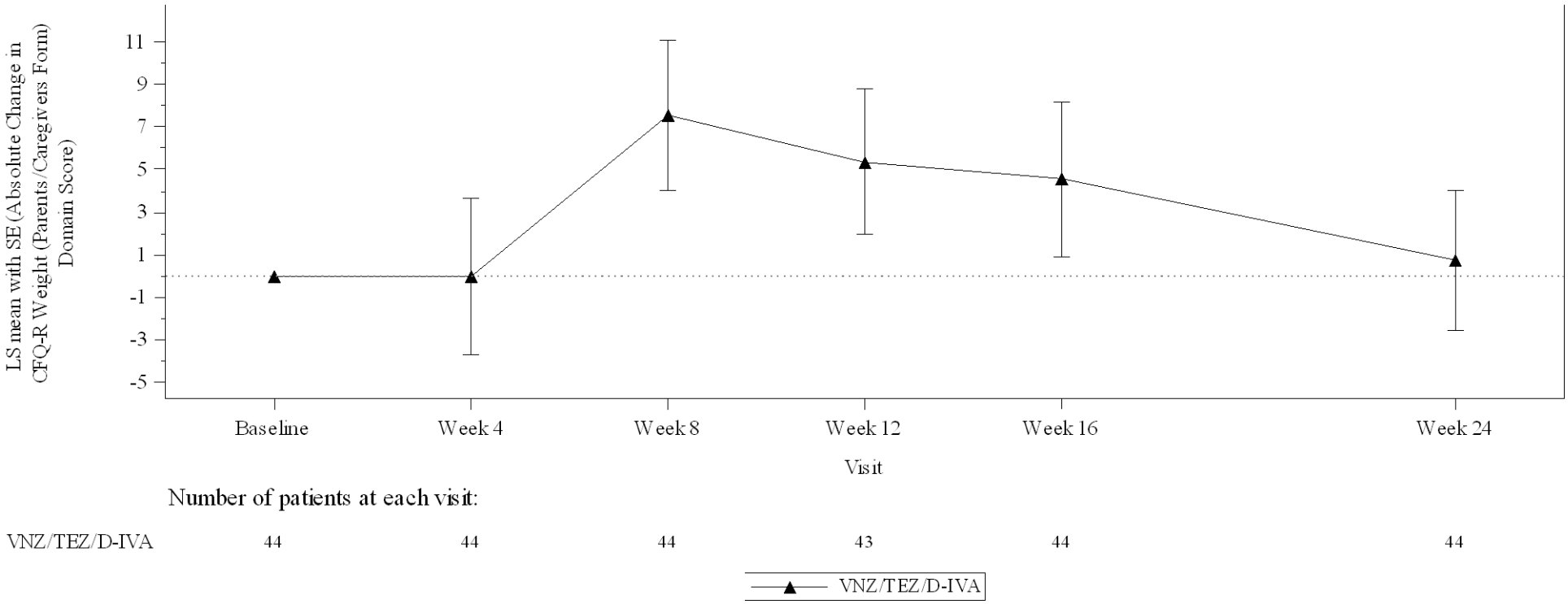
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

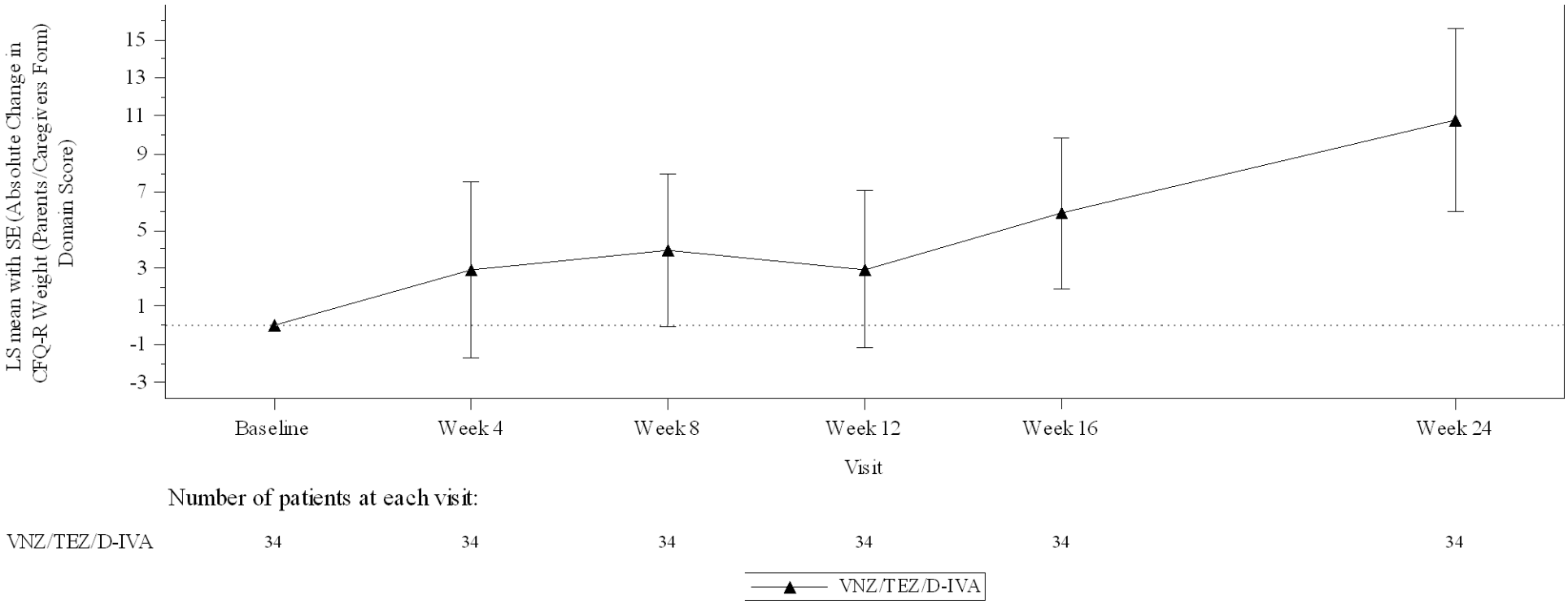
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

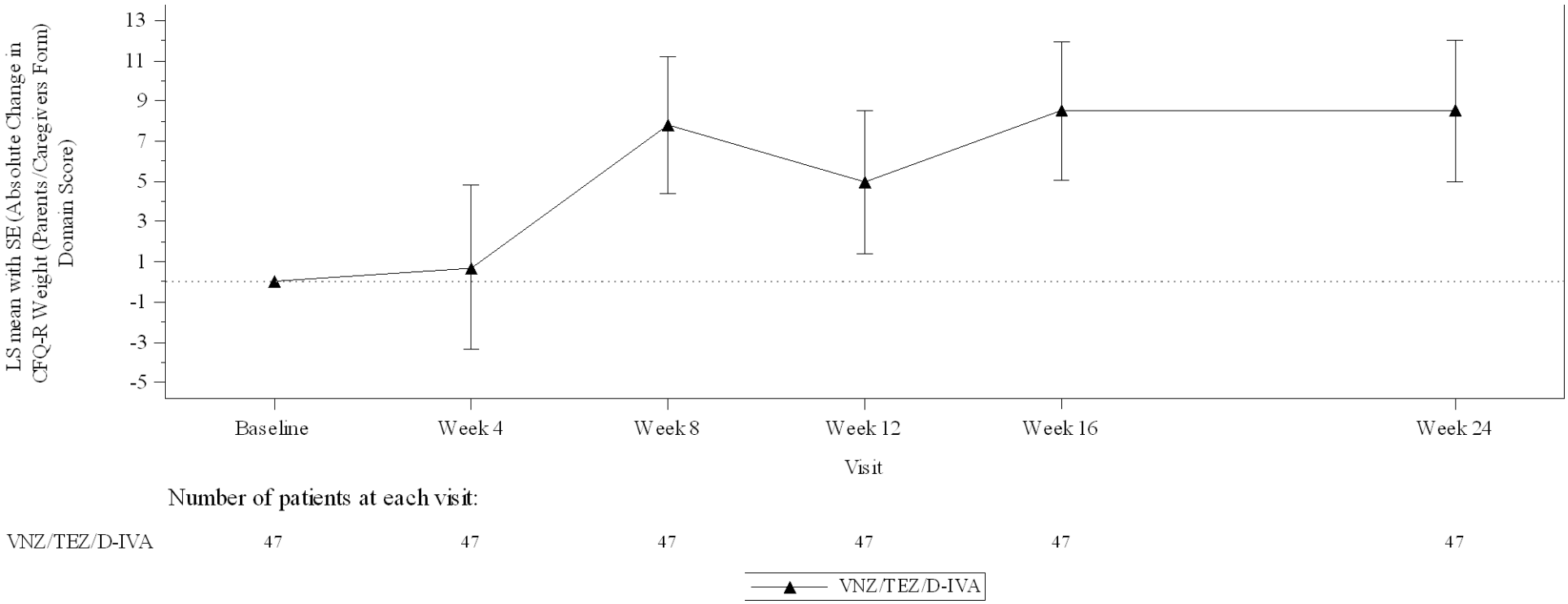
Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Region = North America



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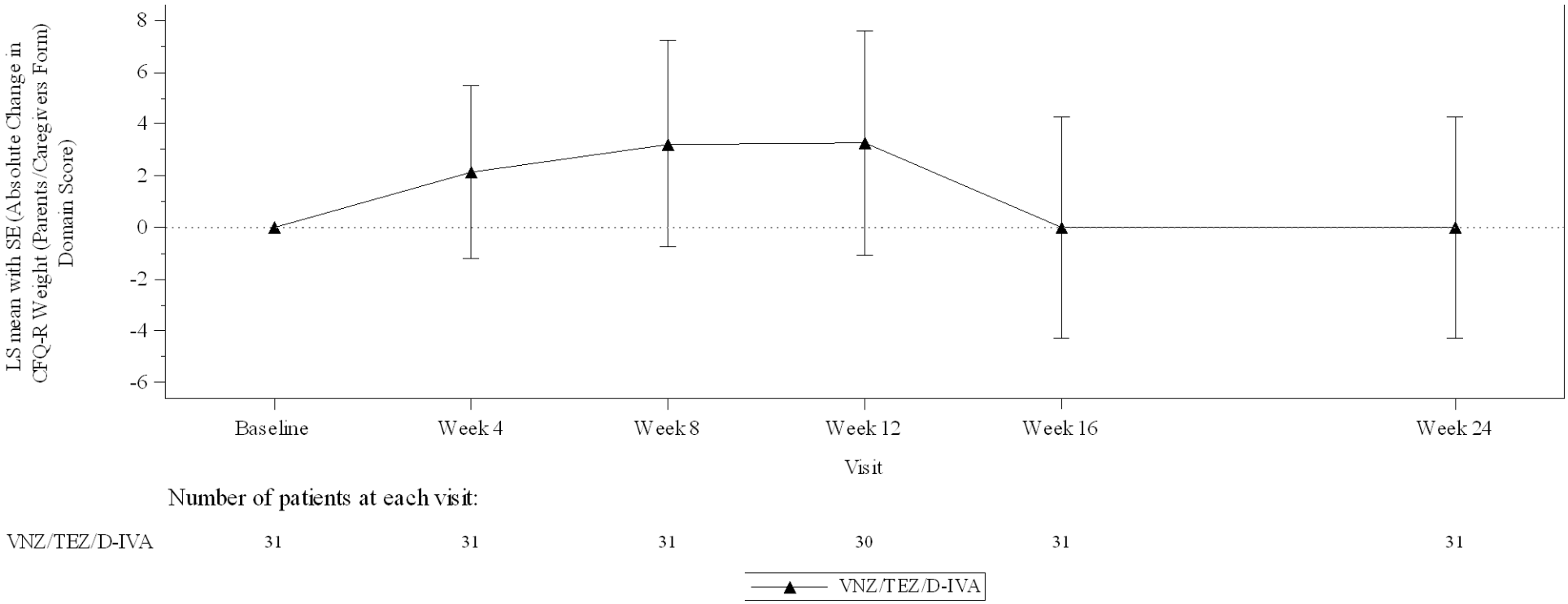
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Region = Rest of World



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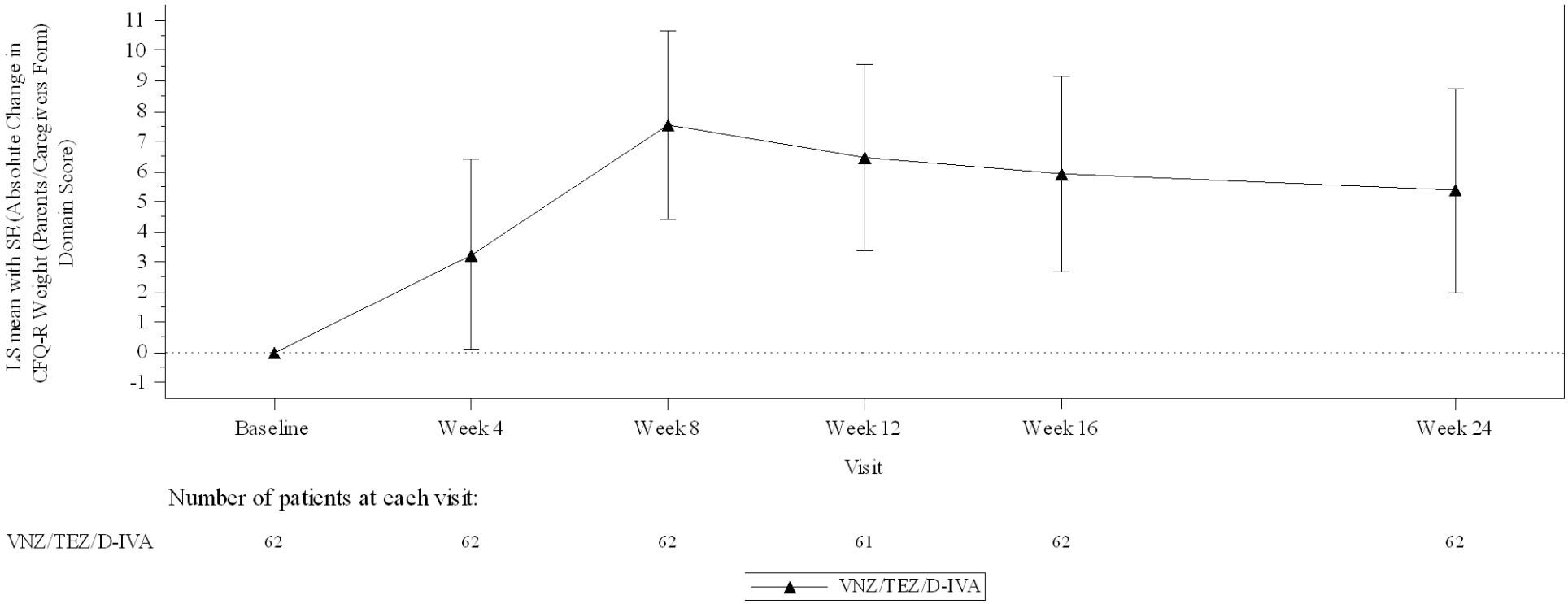
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5



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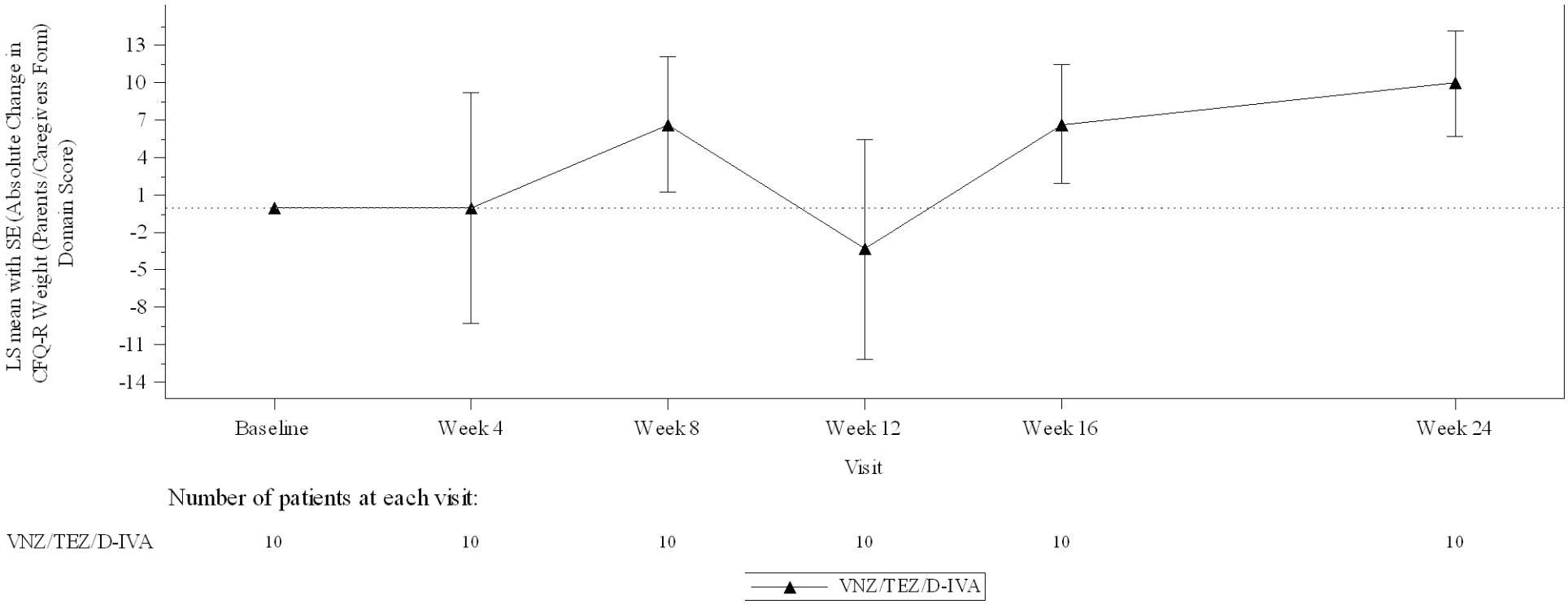
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-qs-abs-cfqr-pa-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5



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- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

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Figure 3.2.2.14.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 3.2.2.14.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 3.2.2.14.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
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Figure 3.2.2.14.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = Rest of the World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 3.2.2.14.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 3.2.2.14.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 3.2.2.15.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-hosp-km-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.15.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-hosp-km-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.15.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-hosp-km-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.15.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = Rest of the World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-hosp-km-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.15.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-hosp-km-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.15.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-hosp-km-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.16.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Male

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-iv-km-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.16.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Female

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-iv-km-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.16.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-iv-km-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.16.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = Rest of the World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-iv-km-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.16.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

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Program: GMA\VX121\germandossier\clinstat_prod\121-105\f-ce-pe-iv-km-24wks-sub-b1.sas Creation: 06FEB2025 10:22

Figure 3.2.2.16.3
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

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